The Journal of Pediatrics

VOL. 53 SEPTEMBER, 1958 No. 3

CHRONIC MONOCYTIC LEUKEMIA IN CHILDHOOD

HOWARD A. PEARSON, M.D., AND LOUIS K. DIAMOND, M.D.

BOSTON, MASS.

CHRONIC monocytic leukemia in childhood is uncommon enough to be considered a pediatric curiosity. During the past twenty-five years, about 900 children with leukemia have been seen at the Children's Medical Center. Only two of these cases have been diagnosed as chronic monocytic leukemia. The two cases differed markedly, and prolonged survival in each instance permits their classification as chronic. One case was characterized by an extended spontaneous remission. The other child remained an obscure and perplexing diagnostic problem for many months before the true nature of his disease became manifest. The clinical features and course of these two cases are described and contrasted with the few cases of chronic monocytic leukemia in childhood reported in the literature.

CASE REPORTS

CASE 1.—A 5-week-old white male infant was admitted to the Infant's Hospital on Feb. 13, 1944, because of an unusual rash.

From the Department of Pediatrics, Harvard Medical School, and the Children's Medical Center.

This study was supported by Grant H-2405 from the National Institutes of Health.

He was the firstborn child of 23-year-old parents. There was no family history of blood disease or malignancy. Pregnancy and delivery were normal, and birth weight was 7 pounds 2 ounces. He had seemed entirely normal until 4 days before admission, when a blotchy rash appeared upon his chest. This gradually spread to involve the entire body. On the day of admission, fever and some respiratory difficulty were noticed.

Physical Examination.—The infant was very pale and irritable. He was covered with a diffuse eruption (Fig. 1). The individual lesions were all elevated, some nodular, varying from 1 to 15 mm. in diameter. Their color was a dusky purple which did not blanch upon pressure. The liver was palpated 5 cm. and the spleen 3 cm. below the costal margins. The cervical, axillary, and inguinal lymph nodes were slightly enlarged and firm in consistency.

The peripheral blood values are listed in Table I. Anemia, thrombopenia, and marked elevation in the leukocyte count with 73 per cent monocytes and 9 per cent "blast" forms were present. The monocytes were actively motile and showed typical monocytic morphological features when stained by supravital methods. Lumbar puncture was normal. No growth was obtained from two blood cultures, and urinalysis was normal.

TABLE I. REPRESENTATIVE PERIPHERAL BLOOD VALUES (CASE 1)

DATE	R.B.C.	HGB.	PLATELETS	W.B.C.	META-MYELOS.	BANDS	POLYS.	EOS.	YOUNG LYMPHS.	LYMPHS.	YOUNG MONOS.	MONOS.	"BLASTS"	RETICS.
2/14/44	2.2	6.7	65,000	281,000	1		2	1	12	2	16	57	9	0.3
2/16	3.5	8.6	48,000	269,000										1.1
2/23	3.8	12.7	101,000	30,000	1	3	13		5	13	14	57	4	1.6
2/29	3.8	11.6	148,000	7,000	4	4	2		60	4	10	14	2	
3/7	3.7	11.7	231,000	11,000		2	15	1	30	41	1	10		2.1
4/1	3.4	9.9	212,000	9,700	1	1	33	1	9	47	6		2	2.6
5/13	4.2	13.2	280,000	6,900			35		10	45	5	5		1.6
6/10	4.7	13.8	222,000	8,500										0.5
11/18	5.3	14.8	215,000	13,700		1	22	2	11	54	5	4	1	0.5
2/17/45	5.0	12.9	348,000	9,200		2	10	3	49	21	3	7	5	0.6
9/13	2.7	7.6	17,000	6,400		5	1		17	42	5	25	5	
9/20	2.3	6.4	50,000	5,200		1	11		13	57	2	15	1	
10/11	3.8	11.3	25,000	1,500	3	1	4		36	28		4	24	
10/16	3.5	9.4	56,000	4,200		2		1	50	23	10	13	1	0.3
12/1	1.0			14,500		1	1		23	13	17	20	25	
12/3	2.1	6.4		9,800									"Many"	
12/7	3.4													
12/22	1.5	4.5	14,000	7,600			4		10	46	4	14	22	0.1
12/24	1.3	3.9												
12/26	1.8	4.7	Rare	5,000			2			40	8	15	35	

Hospital Course.—Shortly after admission, the infant developed severe respiratory distress, and for several days his condition was critical. Fine râles were heard throughout the lungs, and chest roentgenogram showed an infiltration in the right cardiophrenic angle as well as considerable broadening of the superior mediastinal shadow. He was treated with oxygen, intravenous fluids, and parenteral sulfadiazine. Three transfusions of whole blood were given. On this regimen, he slowly improved. The fever fell by lysis and his breathing became normal. On the seventh hospital day, a right otitis media spontaneously drained and *Staphylococcus aureus* was cultured from the discharge.

Serial blood counts demonstrated a decreasing leukocyte count and a rise of the platelet level. The skin lesions began to fade, and the liver, spleen, and lymph nodes decreased in size. On March 14, one month after entry, he was discharged from the hospital.

Fig. 1.—Case 1. Six weeks of age. The diffuse and nodular characteristics of the skin lesions are well demonstrated.

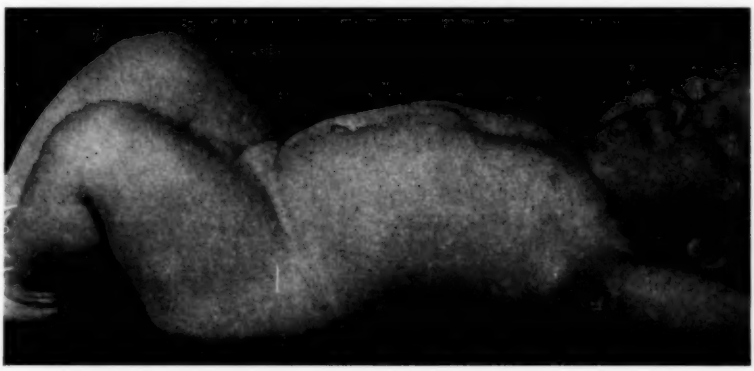

Fig. 2.—Case 1. Nine months of age, during spontaneous clinical remission. Complete clearing of the skin and excellent physical development are apparent.

Except for residual elevated purple skin lesions, he appeared entirely normal. The liver and spleen were both palpated 1.5 cm. below the costal margins.

Subsequent Course.—Two months after discharge, the skin had completely cleared, and liver and spleen were no longer palpable. In September, 1944, when he was 9 months old, he weighed 22 pounds; growth and development were normal (Fig. 2). Examination of the blood showed a persistent 5 to 10 per cent monocytosis with occasional "blast" forms. Because of apparent excellent health, he was not brought to the clinic between February and September, 1945. At this time he again became pale and irritable. On Sept. 10, 1945, he became febrile and started to cough and was readmitted to the hospital the following day.

Second Admission.—He was now a well-developed 20-month-old child. The skin was pale but otherwise clear. The spleen and liver were palpated 3 cm. below the costal margins. A few small cervical lymph nodes were present, but no other adenopathy was noted. Blood counts demonstrated moderate anemia and thrombopenia. Total leukocyte count was not elevated; however, a monocytosis of 30 per cent was present and 5 per cent "blast" forms were counted.

He was irritable and required nearly constant sedation. The hemoglobin level fell rapidly and two blood transfusions were administered. Mild pneumococcal bronchopneumonia was detected and treated with penicillin and sulfadiazine. The pneumonitis slowly resolved and no further transfusions were necessary. After five weeks he had improved sufficiently to be discharged, on Oct. 16, 1945.

For about six weeks he did well at home. Then he became anorectic, irritable, and refused to walk. He was admitted for the third time on Dec. 1, 1945, when he was 23 months old.

Third Admission.—He was extremely pale. The heart was slightly enlarged and a loud hemic murmur was heard over the precordium. The liver was firm, with a sharp edge palpable 4 cm. below the costal margin. The splenic tip was hard and smooth and descended 3 cm. below the left costal margin. Five hundred cubic centimeters of whole blood were given in divided doses. He was discharged home after one week, appearing somewhat better. However, pallor and irritability soon recurred and he was admitted for the last time on Dec. 22, 1945, at the age of 23½ months.

Fourth Admission.—He was extremely pale and many petechiae and ecchymoses were present. The liver and spleen were firm and palpable 4 cm. below the costal margins. Generalized enlargement of lymph nodes averaging 1.5 in diameter was observed.

Despite transfusions, antibiotics, and other supportive treatment, respiration became progressively more difficult. The temperature curve was septic, with peaks of fever to 105° F. He died 6 days after re-entry, on Dec. 28, shortly before his second birthday. The duration of his disease was nearly twenty-three months.

*Post-Mortem Findings.**—There was extensive infiltration of all of the organs and tissues of the body by large mononuclear cells. These cells had abundant clear purple cytoplasm and large vesicular nuclei, many of which were indented, folded, and reniform. Mitoses were rare. Occasionally, phagocytosed material was present. The liver was twice enlarged by weight; leukemic cells were noted infiltrating the capsule and within the sinusoids and in the periportal areas. The spleen was three times heavier than normal, and diffuse replacement of the normal architecture by leukemic

*We are grateful to Dr. John Craig, Pathologist, Children's Medical Center, for review of the autopsy and biopsy material described in this report.

infiltration was present. Massive pulmonary hemorrhages were seen in addition to leukemic infiltration. The marrow spaces of the ribs, sternum, and vertebral bodies were filled with leukemic tissue. The reticulum of spleen and lymph nodes was prominent but not markedly hyperplastic.

CASE 2.—A 10-year-old white boy was referred to the Children's Medical Center on Nov. 29, 1956, because of pancytopenia. His past history was normal and there was no family history of blood dyserasia or malignant disease. He had been entirely well until about 6 months previously when he complained of a painful right knee. He was admitted to another hospital and hemogram and roentgenograms were reportedly normal. His arthralgia rapidly improved and he had no unusual symptoms until 2 months prior to admission, at which time he developed fever and a stiff neck. Leukocyte count was low and erythrocyte sedimentation rate was increased. Rheumatoid arthritis was considered as a possible diagnosis. Serial blood counts demonstrated a progressive lowering of all of the formed elements of the blood. One per cent "blast" forms were seen in buffy coat preparations on two occasions. Nucleated red cells were also noted on peripheral blood smears. Oral ferrous sulfate was prescribed without improvement of the anemia; and because of persistent pancytopenia, he was referred to the Hematology Clinic of the Children's Medical Center.

The boy was pale. The liver edge was palpable 3 cm. below the costal margin, and the tip of the spleen could be felt upon deep inspiration. Peripheral blood studies are outlined in Table II. A macrocytic anemia with a mean corpuscular volume of 105 was found and 16 nucleated red cells per 100 leukocytes were seen. Seventy-five per cent of the nucleated red cells were abnormal forms resembling megaloblasts. Iliac bone marrow aspiration (Table III) showed marked erythroid hyperplasia with moderate megaloblastic changes. Leukocytes and megakaryocytes were normal. Since the family operated a fish market and the patient had handled raw fish, fish tapeworm infestation with secondary megaloblastic anemia was considered a possible diagnosis. He was treated with Atabrine, oral folic acid and parenteral vitamin B_{12}. Stool examinations revealed no ova of *Diphyllobothrium latum*. A slight rise in the hemoglobin level occurred without significant change in the leukocytes or platelets. He was hospitalized at the Children's Medical Center for five days in January, 1957. The serum levels of folic acid, ascorbic acid, iron, and bilirubin were all within normal limits. Free hydrochloric acid and intrinsic factor were present in gastric secretion after histamine administration. Serum vitamin B_{12} was elevated to 675 meg. per cent, but this was considered secondary to the parenteral therapy. Bone marrow aspiration again revealed erythrocyte hyperplasia with persistent megaloblastic changes. From February through June, 1957, he was hospitalized for a total of 86 days. Various regimens of folic acid, vitamin B_{12}, ascorbic acid, crude liver, and fresh plasma were administered without definite hematologic response. Repeated bone marrow aspirations showed no significant changes during this period. A slight rise in the leukocyte and reticulocyte count was recorded during a 10-day course of prednisone administration; however, simultaneously he developed a staphylococcal paronychia and a moderate bronchopneumonia. During April, 1957, and thereafter, a few "blast" forms were occasionally noted in the peripheral blood. Fluctuating normoblastemia was also recorded. In May, platelet survival study demonstrated markedly shortened survival of transfused platelets. Transfusions with packed red cells were necessary each month to maintain the hemoglobin level. Coombs' test was repeatedly negative.

TABLE II.—REPRESENTATIVE PERIPHERAL BLOOD VALUES (CASE 2)

DATE	HGB.	PLATELETS	W.B.C.	META-MYELOS.	BANDS	POLYS.	EOS.	YOUNG LYMPHS.	LYMPHS.	YOUNG MONOS.	MONOS.	"BLASTS"	N.R.B.C. 100 W.B.C.*	RETICS.
6/26/56	12.8	Normal	5,000			48			52					
9/17	11.9		3,500									(1%—Buffy coat prep.)		
9/28	8.7	Decreased	3,100	1	6	47			45		1		2	
11/29	9.0	51,000	2,900		5	42		8	35		10		16	4.8
1/18/57	9.9	27,000	1,800		6	60		9	10		14	1	1	3.4
2/25	10.8	33,000	1,650	2	4	30	2	6	46		10		2	3.6
3/20	10.8	48,000	2,270		8	56		4	26		6			5.3
4/ 8	8.6	34,000	2,950		8	33		7	37	2	7	6	14	5.5
4/26	10.5	40,000	4,000		4	30		12	36	8	6	4	24	13.0
5/24	7.9	70,000	1,320		2	40		20	18		20		1	2.7
6/27	12.5	24,000	1,100		2	23		13	16		46		4	1.6
7/29	8.2	12,000	2,100		6	20		2	36		36		2	1.0
8/19	11.6	17,000	12,700		4	41		9	21		25			0.2
8/22	12.0	20,000	8,900		2	36		2	11		49		64	1.8
9/12	11.1	26,000	17,900		3	25		7	11		54		147	2.2
9/23	9.7	27,000	12,900		4	17	1	3	26	3	40	6	78	1.6
10/21	8.2	5,000	26,800		1	22		1	6		66	4		0.0
10/29	10.6	18,000	33,000		2	23			14	29	27	5	13	
11/29	8.2	36,000	44,000	2	2	13			4	33	40	5	3	
12/23	5.5	12,000	6,000		8	66			1	10	15		4	
1/ 6/58	5.6	13,000	5,300	2	4	12			5	31	41	5		
1/ 9	7.0		2,800											
1/12	6.6		750											

*Nucleated red blood cells per 100 white blood cells.

TABLE III. SELECTED MYELOGRAMS (CASE 2)

DATE	"BLASTS"	MYELO-CYTES	META-MYELOS.	BANDS	POLYS.	LYMPHS.	MONOS.	PROERYTH-ROBLASTS	ERYTHRO-BLASTS	NORMO-BLASTS	COMMENTS
11/29/56	1.0	5.0	12.0	6.0	2.0	1.0	0.0	16.0	17.0	40.0	Hypercellular marrow. Marked erythroid hyperplasia with megaloblastic changes. Megakaryocytes normal. E:M = 3:1
5/ 8/57	0.5	4.0	11.0	4.0	3.5	5.5	1.5	17.0	28.0	25.0	Hypercellular. Erythroid hyperplasia with megaloblastic changes. Megakaryocytes adequate. E:M = 3:1
8/ 8/57	3.0	11.0	13.0	4.0	10.0	18.0	22.0	1.0	7.0	11.0	Hypercellular with myeloid predominance and monocytosis. Megakaryocytes adequate. Slight megaloblastic changes
10/22/57 (Postsplenectomy)	18.0		6.0	7.0	15.0	3.0	48.0		1.0	2.0	Hypercellular. Absent megakaryocytes and marked reduction of erythroid elements. Marked monocytosis. "Blasts" increased

In early June, 1957, he developed multiple painful abscesses of the antecubital spaces, legs, and buttocks (Fig. 3). Cultures were positive for hemolytic *Staphylococcus aureus* and *Proteus vulgaris*. The lesions progressed into chronic ulcerations; however, biopsy was interpreted as showing only nonspecific granulation tissue surrounding an infected ulcer.

Coincidental with the appearance of the skin lesions the leukocyte count began to rise, with an increasing percentage of monocytes. These cells were large and had gray-blue cytoplasm. A few had irregular outlines suggesting pseudopodia. Many reddish-purple granules were present in the cytoplasm. The nuclei had a feathery chromatin pattern. Many nuclei showed extreme convolutions and had a transparent quality. The peroxidase reaction was slightly positive in most cells. In wet preparations they were actively motile and phagocytosed particles of India ink. In August it became necessary to transfuse the boy even more frequently, and the level of indirect bilirubin in the serum was elevated to 7.9 mg. per cent. Bone marrow aspiration on Aug. 8, 1957, showed only 3 per cent blast forms, and, although the monocytes were 22 per cent, it was not considered diagnostic of leukemia. Megakaryocytes were seen in normal numbers.

Because of the evidence of increased hemolysis and increased platelet destruction, a splenectomy was performed on Aug. 20, 1957. The spleen was enlarged to 165 grams (normal 80 grams). The red pulp demonstrated a pleomorphic hypercellularity with many monocytes and occasional reticulum-type cells. This was considered consistent with monocytic leukemia.

Postoperatively, marked leukocytosis, monocytosis, and normoblastemia were observed. However, the platelet count remained depressed, and frequent transfusions were necessary because of recurring anemia. "Blast" forms were observed regularly in the peripheral blood.

Fig. 3.—Case 2. Chronic infected ulceration of anticubital space.

The skin lesions were extremely difficult to manage. Topical silver nitrate was only temporarily effective in decreasing the exophytic granulation tissue which developed. In September, 1957, after approximately 300 r of superficial x-ray therapy, the rapid growth of the lesions seemed checked.

A bone marrow aspiration done on Oct. 22, 1957, showed 18 per cent "blast" forms and 48 per cent monocytes, and, for the first time, the diagnosis of monocytic leukemia could be established by marrow study. The child was transferred to the Tumor Therapy unit* and treatment with 6-mercaptopurine and triamcinolone

*We are indebted to Dr. Sidney Farber and members of his unit for details of his care and course there.

was instituted. Little change was observed in the peripheral blood counts. Marked gingival hypertrophy and ulceration developed, and the gingiva separated from the teeth exposing dentin and roots. X-ray therapy had only a slight effect on the buccal process. The older cutaneous lesions progressed into large, flat indolent necrotic areas. New lesions developed on the wrists, ankles, and on the eyelids. *Staphylococcus aureus* and *Proteus vulgaris* were consistently recovered from these. The child lost weight and appeared cachectic. Generalized enlargement of the lymph nodes was observed. The hemolytic anemia became still more severe, and despite weekly transfusions the hemoglobin level remained below 10 Gm. per cent. On Dec. 23, 1957, 6-mercaptopurine was discontinued and treatment with Methotrexate was begun. Firm painful swellings developed in both breasts and spread to involve much of the anterior chest wall. Fluctuation then occurred. The chest roentgenogram demonstrated destruction of the underlying ribs. He had a septic spiking temperature despite massive doses of intravenous Chloromycetin and ACTH. The respirations became very labored; he lapsed into coma and shock and died on Jan. 12, 1958. Terminally he developed marked leukopenia. The duration of the boy's illness was at least 16 months.

Post-Mortem Findings.—The body was wasted and had marked Cushingoid features. In addition to extensive cutaneous ulcerations, large fluctuant masses underlying the breasts were observed. Incision of these revealed large collections of pus with dissection throughout the tissues of the chest wall down to the parietal pleura. The costochondral junctions were nearly completely destroyed by abscess formation. Extensive osteomyelitis of the ribs was observed microscopically.

The liver was 2½ times enlarged and microscopically demonstrated monocytic infiltration of capsule and periportal areas. Hemosiderosis and passive congestion were also noted.

Generalized lymphadenopathy was present. Microscopically the normal architecture was replaced by large numbers of leukemic monocytes and hemorrhage. The reticulum was prominent but not markedly hyperplastic.

The heart was dilated and hypertrophied. The lungs were very wet and heavy, and demonstrated hemorrhage, hemosiderosis, pulmonary edema, and chronic pneumonitis. *Staphylococcus aureus* and *Proteus vulgaris* were cultured from the lungs, skin lesions, and chest abcesses. The bone marrow was hypercellular and diffusely replaced by leukemic monocytes and "blasts."

DISCUSSION

The existence of monocytic leukemia as an entity distinct from myelogenous leukemia was first postulated by Reschad and Schilling-Torgau[1] in 1913. Reviews by Dameshek[2] and Clough[3] established the characteristic clinical and morphological features of the disease. By 1942 Evans[4] ascertained that a majority of American and Canadian hematologists agreed that monocytic leukemia, with acute, subacute, and chronic varieties, was a definite entity.

Even today controversy exists concerning the origin of the leukemic cells. Some hematologists follow the precepts of Downey[5] and distinguish two forms of monocytic leukemia. In the Schilling type, the leukemic-endothelial cell precursors and hyperplasia of the reticulum is observed histologically although this feature is not invariable.[2] In the Naegeli variety, the monocytes are believed to be developmental products of myeloblasts, and young cells of the myelocytic series are observed in large numbers.

A relationship between monocytic leukemia and malignant proliferative reticuloendotheliosis[6, 7] or "atypical" Letterer-Siwe's syndrome[8] has been postulated, for in some of these cases large, abnormal histiocytes may be seen in the peripheral blood.

Whatever may be the origin of the leukemic cells in a specific case of chronic monocytic leukemia, a characteristic blood picture is observed. The peripheral blood and marrow contain varying numbers of cells which resemble adult monocytes and their precursors. These cells have clear, gray-blue cytoplasm containing myriads of reddish-purple granules. The nuclei have a fine meshed chromatin and vary in shape. A markedly convoluted nucleus with a thin "cellophane" quality is often seen.[9] The monocytes are actively motile, and this is reflected in cytoplasmic projections or pseudopods seen on the stained smear. Active phagocytosis may be observed. The peroxidase reaction is usually positive but less marked than that of cells of the granulocytic series. Episodic outpourings of large numbers of immature cells of the myelocytic series is often seen, and this may cause some diagnostic confusion. Erythroblastemia of varying degrees is usually observed.[10]

In 1937 Osgood[10] collected 127 cases of monocytic leukemia from the world literature, and this group included 14 children whose cases were documented well enough to evaluate. The disease was acute in 13 of these. The acute form also predominated in 13 cases followed at the Children's Medical Center during the past 25 years, for 11 of the 13 cases classified as monocytic leukemia were of the acute variety. These children had fulminating disease with purpura, anemia, and extreme toxicity.

Doan and Wiseman[11] described the essential features of the chronic form of monocytic leukemia in 1934. In a 1956 review article, Sinn and Dick[12] listed 14 cases from the literature to which they added 8 of their own. No children were included in this group. These authors emphasized an insidious onset in most cases. Resistant anemia and pancytopenia were frequently the initial manifestation of the disease, and in the early stages the bone marrow findings were not diagnostic of leukemia. They believed that a "preleukemic" onset was characteristic of chronic monocytic leukemia in adults, although a similar course may be seen in other forms of leukemia.[13]

In 1934 Foot and Olcott[14] described the pathologic features of a case which has generally been accepted as chronic monocytic leukemia. Although the clinical summary is very brief, their patient, a 3-year-old white girl, had pallor and a petechial eruption for about a year before being studied. The child had peripheral pancytopenia without leukemic changes and moderate enlargement of spleen and liver. A splenectomy was performed, and four months later the child succumbed to staphylococcal septicemia. At autopsy, extensive monocytic infiltration of the tissues and bone marrow was observed. In 1939 Court and Edward[15] reported a case of monocytic leukemia in a 5-year-old white boy. The child was pale and had increased susceptibility to infection for about nine months. Examination of the blood revealed pancytopenia with monocytosis. During the last two months of

life purpura and ulcerative stomatitis developed. Widespread infiltrations of monocytes and monocytic precursors were observed at autopsy. Hyperplasia of the reticulum was not striking. A recent article by Stransky and Reyes[16] described a 3-year-old girl with monocytic leukemia which the authors classified as chronic. However, the duration of the disease is uncertain. Marked lymphocytosis with monocytes never exceeding 3 per cent was observed in the peripheral blood. None of these cases had the massive splenomegaly and peripheral blood picture which are characteristic of chronic myelogenous leukemia in the pediatric age group.[17]

Our cases illustrate two different clinical varieties of chronic monocytic leukemia. The first type, as in Case 1, might be termed an acute remitting variety. The child presented with the findings suggestive of acute leukemia. A striking feature was extensive infiltration of the skin. Montgomery and Watkins[18] emphasized the cutaneous manifestations of monocytic leukemia and postulated a primary autochthonous cutaneous origin in some cases. A spontaneous remission occurred during which the child appeared entirely well; the blood picture returned toward normal. Remission in this case lasted about eighteen months. Much shorter remissions have been observed in several cases and these have generally followed acute infections.[15] Similar remissions are occasionally seen in adult cases, Schiro and Weiss[19] reporting one of at least 4 years' duration.

The clinical course in Case 2 was very different and resembles some of the cases reported by Sinn and Dick.[12] A striking feature early in the course of this case was moderate anemia with megaloblastic changes of the peripheral blood and bone marrow. This led to protracted trials with various specific hematinics. Many cases of leukemia have been reported in adults in which the presenting manifestation was a megaloblastic or pernicious anemia-like picture, the so-called leukanemia.[12, 20, 21] It is believed that abnormal red cell maturation results from depletion of metabolic factors by rapidly growing malignant tissue.[22, 23] There was also marked increase in susceptibility to skin infection which was out of proportion to the degree of granulocytopenia observed. Later, persistent pancytopenia combined with a cellular, nonleukemic bone marrow, in addition to other evidence of hemolytic anemia and decreased platelet survival, suggested the possibility of a hypersplenic state. Accordingly, splenectomy was performed. After operation the peripheral blood and bone marrow demonstrated unequivocal leukemic changes. Whether removal of the spleen permitted the process to become overt is speculative. Even early in this child's disease, "blasts" forms were observed occasionally in the peripheral blood, suggesting a malignant process from the start. However, repeated bone marrow aspirations from several sites showed no definite malignant changes until almost terminally. It may be inferred that the earliest anaplastic changes occurred elsewhere in the reticuloendothelial system. Relatively late in the disease the bone marrow became involved, and only at this time could the diagnosis of monocytic leukemia be unequivocably established.

SUMMARY

Two cases of chronic monocytic leukemia in childhood are described. The first patient, an infant, had a prolonged spontaneous remission before succumbing to the disease. The second child was especially baffling because of chronic skin infections and severe pancytopenia. Megaloblastic changes were noted in the cells of the erythrocytic series. No response was obtained by treatment with several hematinics, especially vitamin B_{12} and folic acid. Evidence of hemolytic anemia and shortened platelet survival suggested a "hypersplenic" mechanism. Splenectomy did not ameliorate the pancytopenia. On the contrary, the previously aleukemic process became overt after the operation.

The long remission without specific antileukemic therapy in Case 1 suggests the necessity for caution in interpreting as specific the occasional responses to chemical agents in chronic monocytic leukemia. Case 2 re-emphasizes the dictum that leukemia may be the underlying diagnosis in bizzare and obscure hematologic pictures.

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THE SALICYLATE PROBLEM WITH SPECIAL REFERENCE TO METHYL SALICYLATE

HOWARD M. CANN, M.D., AND HENRY L. VERHULST, M.S.
WASHINGTON, D. C.

WITH the report of the recent death of three children from accidental ingestion of methyl salicylate (wintergreen oil), it is timely to discuss the problem of salicylate intoxication.

Poisoning from all salicylates is a serious health problem in children. In 1956, 18 per cent of all accidental poisoning deaths in children under 5 years of age were due to salicylates.[1] Salicylates were second only to petroleum products as the main cause of accidental poisoning death in this age group.

Jacobziner,[2] reporting on 454 cases of poisoning in children under 16 years of age, found that salicylates accounted for 16.5 per cent of the cases. Of 3,926 accidental ingestions reported to this office by 29 poison control centers in the eastern and midwestern United States, 25 per cent was caused by accidental ingestion of salicylates (Table I). These cases occurred in various time periods between July, 1956, and April, 1958.

Special studies[3] have shown that there were 28 deaths from accidental ingestion of methyl salicylate in 1951 and 34 deaths in 1952 in this country (Table II).

TABLE I. NUMBER OF SALICYLATE INGESTIONS REPORTED BY 29 POISON CONTROL CENTERS

TYPE OF SUBSTANCES INGESTED	NUMBER	PER CENT
Total	3,926	100.0
Total salicylates	1,004	25.6
Aspirin	983	25.0
Methyl salicylate preparations	19	0.5
Salicylic acid	2	0.1

TABLE II. DEATHS FROM METHYL SALICYLATE IN THE UNITED STATES[3]

Years	1951	1952
Fatalities	28	34*

*Of those cases in which amounts ingested were reported, a death resulted in a 1-year-old child following ingestion of 4 ml. methyl salicylate.

The widespread use of acetylsalicylic acid, the extreme toxicity of methyl salicylate, and the public's unawareness of the toxicity of these substances are probably the main reasons for the extent of the problem.

In 1956 Done and Otterness,[4] in an excellent paper concerning methyl salicylate poisoning, stated: "Despite numerous reports of fatalities from ingestion of very small amounts of this substance (methyl salicylate), its toxicity is poorly appreciated both by physicians and the laity." Apparently

National Clearinghouse for Poison Control Centers, Accident Prevention Program, Public Health Service, U. S. Department of Health, Education, and Welfare.

the toxicity of wintergreen oil is still poorly appreciated in some areas, as the three following cases reports indicate.

CASE REPORTS

CASE 1.—A 2½-year-old boy ingested about ½ ounce of methyl salicylate from a bottle on a table near his mother's bed. The label of the bottle contained the warning *"Poisonous if Taken Internally. Keep Out of the Reach of Children."* Upon discovering the ingestion, the boy's mother called the drugstore where the product was purchased. She was advised to give her son water and to call her physician. Her physician, who returned the call 25 minutes later, suggested the boy be given burnt toast, milk of magnesia, and strong tea. The boy vomited twice in the 12 hours following ingestion. Fourteen hours after ingestion the boy began frothing from the mouth and was taken to the hospital. Treatment was started but the patient expired.

CASE 2.—A 2-year-old boy ingested about ½ ounce of methyl salicylate from a bottle marked *"Caution. Keep Out of Reach of Children."* Upon calling their physician, the parents were advised to keep the boy quiet and covered with blankets. Soon they had to call the fire department because the boy was having breathing difficulties. The firemen, using a resuscitator, revived the boy. When the family physician arrived at the home 1½ hours after the ingestion, the boy was rushed to the hospital. He died that same day in the hospital.

CASE 3.—A 2½-year-old girl was accidently given 1 teaspoon of methyl salicylate instead of a cough medicine. The methyl salicylate and cough medicine were stored in bottles of the same size, color, and shape. The bottles were properly labeled as to ingredients. When the child showed signs of distress, her father called a physician who prescribed liquids. The father then took her to the hospital, where, despite excellent medical care, she died.

COMMENTS

In the first two cases, it is significant that although the methyl salicylate bottles were marked *"Keep Out of the Reach of Children,"* the warning was not heeded.

A physician was contacted in each case, in the first two instances before symptoms had occurred. In none of these cases were immediate attempts made to empty the stomach and proper therapy was delayed.

In the third case, similarity of a methyl salicylate container and a cough medicine container, despite proper ingredient labeling, was apparently the cause of the fatal accident.

DISCUSSION

Such factors as the pleasant odor and the high concentration of salicylate in this preparation make methyl salicylate an especially hazardous substance to children. A teaspoon of wintergreen oil contains 45 grains of salicylate,[5] an amount which may be fatal in children.[6]

Although methyl salicylate is hydrolyzed in the stomach to form methyl alcohol and salicylic acid, it is doubtful that the methyl alcohol formed contributes to the intoxication.[5] Wintergreen oil poisoning is primarily a salicylate poisoning caused by ingestion of a substance containing about 90 per cent salicylate, and the toxic manifestations which result are identical to those of poisoning from other salicylates.

The public should be advised of the toxicity and lethal potential of wintergreen oil. Proper labeling is apparently not enough. Case 3 certainly points out the danger of storing internal and external medications together.

The advice to call a physician at once in the event of an accidental ingestion of a toxic or potentially toxic substance cannot be overemphasized (especially when the ingested substance is methyl salicylate).

cent of 983 cases of acetylsalicylic acid ingestion in a series of 3,926 reports of ingestion submitted to this office by 29 poison control centers in the eastern and midwestern United States (Table III).

TABLE III.—CASES OF ASPIRIN INGESTION REPORTED FROM TWENTY-NINE POISON CONTROL CENTERS

ASPIRIN	NUMBER	PER CENT
Total	983	100
"Baby"	611	62.1
"Adult"	109	10.9
Unspecified	263	26.3

When a child has accidentally ingested a salicylate product, treatment should be started as soon as possible. *In all cases the stomach must be emptied promptly.* Mild intoxication can often be remedied by this procedure. If gastric lavage is performed, sodium bicarbonate should not be used, since it enhances salicylate absorption from the gastrointestinal tract. Methyl salicylate delays stomach emptying; gastric lavage may, therefore, be carried out as long as 4 to 6 hours after its ingestion.[6, 7]

There are some who advise hospitalization of most cases of salicylate ingestion whether or not symptoms have occurred—if only for overnight observation. Such practice emphasizes the necessity of prompt, vigorous therapy and close observation in all instances of salicylate overdosage. In methyl salicylate poisoning the usual asymptomatic period following ingestion makes prolonged close observation mandatory.

With the introduction of flavored aspirin tablets, the incidence of salicylate poisoning in children has probably increased, but reports from poison control centers indicate that unflavored aspirin tablets still account for many cases of salicylate poisoning. Regular "adult" aspirin caused about 11 per

Rational management of salicylate poisoning is based on a thorough understanding of the pathophysiology induced by the salicylates. Until recently there had been some confusion as to the acid-base disturbances occurring in acute salicylism. However, if one follows the pH of the blood, it is quite obvious that an alkalosis occurs initially. Salicylate stimulation of the respiratory center produces hyperpnea resulting in a carbon dioxide deficit. Renal compensation by bicarbonate excretion facilitates the development of acidosis. Salicylates affect carbohydrate metabolism. It is believed that an abnormal production and accumulation of organic acids occur. In order for the kidney to excrete these end products, fixed base must also be excreted. Acidosis results. Furthermore, it has been shown that salicylates in the concentrations usually found in the plasma during poisoning can inhibit the first two steps of the Krebs tricarboxylic acid cycle.[8] The ketosis which results from disruption of this cycle and from starvation may contribute to the acidosis.

In acute salicylate intoxication, water is lost from the body by diaphoresis and by hyperpnea. Antecedent or coincident vomiting or diarrhea increases

body water deficit with impaired renal function and decreased salicylate excretion. The possibility of a vicious cycle is quite evident.

The hypoprothrombinemic effect of salicylates is well known. The plasma fibrinogen[7, 9] may become depressed, and widespread capillary damage may also result from salicylate intoxication.

Vomiting followed by hyperpnea is most frequently seen in acute salicylism. Hyperpyrexia, sweating, convulsions, delirium, or coma may also ensue. Elevated blood salicylate concentrations support the diagnosis, but low blood concentrations do not rule out the diagnosis. Severe intoxication in patients with low salicylate blood levels has been reported not uncommonly. Thus, the diagnosis is made on a clinical basis.

The treatment of established salicylate intoxication consists of giving fluids intravenously (orally in mild cases) to correct the existing water deficit and maintain adequate urinary output; glucose may be of value in combating ketosis and should be given. During the early alkalotic stage hypotonic saline solutions may be given; base therapy during this stage may lead to tetany, convulsions, and death. Only after acidosis supervenes (usually 6 to 8 hours after toxic signs and symptoms have appeared) should base (sodium bicarbonate or sodium lactate) be administered. There are some, however, who feel that administration of sodium bicarbonate is not harmful even when given early in the course of the development of symptoms.[8] It has been shown that the renal clearance of free salicylate is increased in the presence of an alkaline urine.[6] Thus correction of the acidosis and increased excretion of salicylate result from base administration. However, the base must be administered cautiously and in small doses. Attempts at rapid correction of the acidosis may result in alkalosis.

Vitamin K_1 adequately deals with hypoprothrombinemia. Ascorbic acid may be of value for any capillary damage that occurs.

Barbiturates, paraldehyde, and morphine are contraindicated. A synergistic effect has been demonstrated between these drugs and salicylates, resulting in central nervous system depression.[7, 10] If convulsions occur, oxygen administration may be of some help.[7] Tetany is best treated by intravenous calcium gluconate.

Hemodialysis has been used for treating acute salicylism.[9, 11] Abel and associates,[17] in 1914, in work with the first artificial kidney, used salicylic acid as the substance to be cleared from the blood stream of experimental animals.

Although it has been shown that salicylates are bound to plasma proteins,[12, 13] good clinical results have been obtained with hemodialysis. Furthermore, in vitro dialysis demonstrates that salicylic acid is cleared from both saline and plasma at almost the same rate.[10] Doolan and his associates[11] have shown that hemodialysis removes salicylate from the blood stream five to seven times faster than the normal kidney. They recommend early hemodialysis for severe salicylate intoxication. Once the drug is fixed to the tissues, hemodialysis will be less effective.

In those cases of severe acute salicylism treated by the artificial kidney,

the increased respiratory rate and excursion have been noted to decrease during the procedure, and coma has been reversed.

blood was required for exchange transfusion in this case; 1,345 ml. was used in the case reported by Done and Otterness.

TABLE IV. EXCHANGE TRANSFUSION FOR ACUTE SALICYLISM

	DONE AND OTTERNESS[4]	ADAMS, BIGLER, AND GREEN[5]	DIAMOND AND DE YOUNG[14]
Age of Patient	24 months	20 months	24 months
Amount of blood used	1,345 ml.	2,035 ml.	1,270 ml.
Blood concentration before transfusion	84 mg./100 ml.	72 mg./100 ml.	96 mg./100 ml.
Blood concentration after transfusion	51 mg./100 ml.	29 mg./100 ml.	58 mg./100 ml.

The acid-base disturbance encountered in severe acute salicylism will also be remedied during the procedure. Circulating ketone bodies along with salicylate will be removed from the blood. Electrolyte deficiences will be repaired by adjusting the content of the rinsing fluid accordingly.

Exchange transfusion has been used in cases of methyl salicylate poisoning with favorable results.[4, 5, 14] In the case reported by Done and Otterness,[4] a threefold increase in the rate of salicylate elimination occurred when exchange transfusion was employed in a 2-year-old child for methyl salicylate intoxication. Hyperpnea was reduced markedly following the transfusion and a blood salicylate concentration of 84 mg./100 ml. at the start of the procedure was reduced to 51 mg./100 ml. at the conclusion of the procedure.

Adams and his co-workers,[5] employing exchange transfusion in a 20-month-old child, comatose from ingestion of methyl salicylate, succeeded in lowering the blood salicylate concentration from 72.7 mg./100 ml. to 29.8 mg./100 ml. Although hyperpnea was evident at the conclusion of the procedure, the child's level of consciousness was improved over that prior to the procedure. A total of 2,035 ml. of

Table IV summarizes these two cases and another recent case[14] in which exchange transfusion was employed. Note that a total of 1,500 ml. of blood is required for hemodialysis in adults with the disposable coil type of artificial kidney; less blood is required for the procedure in children.[15]

Since removal of solute (in this case salicylate) from the circulating blood volume is achieved by either hemodialysis or exchange transfusion, the choice of procedure depends on such factors as availability of hemodialysis facilities and the age and weight of the child. If an artificial kidney operated by an experienced team is not readily available, exchange transfusion becomes the more obvious choice. If artificial kidney facilities are close at hand and the patient is an older child or adult, hemodialysis seems to be the preferred procedure. In older children and adults, smaller amounts of bank blood are required to prime the artificial kidney than are needed for exchange transfusion. However, in infants the smaller circulating blood volume permits employment of exchange transfusion or hemodialysis. More and more experience with hemodialysis is being gained and there are artificial kidney centers throughout the country.[16]

Certainly one of these procedures should be considered in patients with salicylate intoxication who are comatose, who exhibit severe neurological manifestations, or whose clinical condition is deteriorating in the face of supportive therapy.

CONCLUSION

Prevention is much preferred to treatment, but where ingestion has occurred prompt emptying of the stomach and observation are indicated, as is early institution of therapy in established cases of acute salicylism.

Any ingestion of methyl salicylate should be considered a medical emergency because it is so toxic. Wintergreen oil delays stomach emptying; thus gastric lavage may be used effectively up to 6 hours following ingestion and should be performed. The lack of symptoms following ingestion does not necessarily indicate a favorable prognosis. After emptying the stomach, the patient should be closely observed for the next 24 hours. In severe cases of salicylism, the use of the artificial kidney or exchange transfusion should be considered. It is hoped that in following these principles the morbidity and mortality from salicylates may be significantly reduced.

We wish to thank the Food and Drug Administration of the United States Department of Health, Education and Welfare for permission to use the case reports contained herein.

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HYDRAMNIOS AS A SIGNAL TO THE PHYSICIAN RESPONSIBLE FOR NEWBORN INFANTS

VERNON R. DEYOUNG, M.D.
CHICAGO, ILL.

THAT the gastrointestinal and possibly the respiratory tracts of the fetus serve as absorbers of amniotic fluid is of more than academic interest in relation to the circulation of the amniotic fluid. Abnormalities of this function produce hydramnios which, if properly interpreted, can point to reparable defects in the newborn infant early enough to save life.

This observation was first made by Mengert and Bourland,[1] who presented it as evidence for the better understanding of the origin and circulation of the amniotic fluid. However, its diagnostic significance was not emphasized. Only recently has hydramnios in relation to the newborn infant been mentioned in the literature as a practical diagnostic sign.[2-4]

To be able to appreciate hydramnios as a diagnostic sign, the highlights of the development of the knowledge of intrauterine fetal alimentary activity are first in order. It had long been observed that meconium contained amniotic sac contents, such as lanugo hairs and cornified epithelial cells, offering ample proof that the fetus swallowed amniotic fluid. Use of this observation was made by Farber,[5] who noticed that these elements were absent in the meconium of the newborn infant with atresia of the alimentary tract. Experimental work lent insight into this observation. Speert[6] observed fetal swallowing and gastrointestinal activity in the rhesus monkey by means of serial roentgenograms after the injection of radiopaque media into the amniotic cavity. Davis and Potter[7] injected Thorotrast into the amniotic cavity of women in various phases of gestation and removed living fetuses of various ages by hysterotomy. Roentgenograms of these fetuses showed concentration of thorium not only in the gastrointestinal tract but also in the lungs. The clinical observations to be presented are interesting additions to this experimental work.

The diagnostic significance of hydramnios has its greatest value in the early recognition of high obstructions of the newborn infant's alimentary tract. Over a period of twelve years of watching over a nursery service that accommodated approximately 12,000 newborn infants, 8 such situations were encountered (Table I, *A*, *B*, *C*). These defects are responsible for most of the surgery of the newborn period and, on the other hand, for the most discouraging mortality figures of any of the neonatal conditions within the reach of surgical therapy. The reason for this is that usually the surgeon is presented with intestinal obstruction

2334 West 116th Place.

TABLE I. SUMMARIES OF CASES OBSERVED

CASE	SEX	WHEN HYDRAMNIOS WAS FIRST NOTED	AMOUNT OF AMNIOTIC FLUID (ML.) (ESTIMATED)	FIRST SYMPTOMS	FARBER TEST	X-RAY	DISPOSITION
A. Six Cases of Congenital Atresia of the Duodenum Associated With Hydramnios							
1	F	Last trimester	3,000	Vomited bright red blood after first feeding	Not tested	"Hourglass" air bubble. No gas below duodenum	Diagnosed on 6th day. Died 8th day. Autopsy revealed complete atresia at junction of 1st and 2nd portion of duodenum
2	M	Fifth month	5,000	Vomited heavily blood-tinged and green-colored material from first feeding	Positive	Dilated stomach. No gas below pylorus	Diagnosed in 12 hours. At surgery atresia of duodenum 5 mm. distal to pylorus. Gastrojejunostomy. Survived
4	F	Last trimester	4,000	Vomited green material from first feeding	Positive	"Hourglass" air bubble. No gas below 2nd part of duodenum	Diagnosed in 35 hours. At surgery atresia at 2nd part of duodenum. Duodenojejunostomy. Survived
6	M	Last trimester	8,000 to 10,000	Prematurity (1,952 grams). Vomited green material without feeding	Positive	"Hourglass" air bubble. No gas below 2nd part of duodenum	Diagnosed in 12 hours. At surgery atresia at 2nd part of duodenum. Duodenojejunostomy. Died
7	M	Last three weeks	5,000	Vomited everything during first 72 hours. Vomitus green and "coffee grounds"	Positive	"Hourglass" air bubble, plus bubble in pars horizontalis of duodenum. No gas below that bubble	Diagnosed in 72 hours. At surgery atresia of duodenum proximal to jejunum. Duodenojejunostomy. Survived
10	M	Last trimester	4,000	Prematurity (1,980 grams). Mongolism. Systolic murmur at apex. Cyanosis. Vomited bloody material without being fed	Positive	None	Diagnosed in 2 hours. Condition too poor for surgery. Died in 18 hours. Autopsy showed atresia distal to first part of duodenum

B. A Case of Esophageal Atresia With Tracheoesophageal Fistula Associated With Hydramnios							
3	F	Fifth month	3,000	Immediate regurgitation of any fluid fed. Thick mucus in pharynx	Negative	Bubble of gas in stomach, but nowhere else. Catheter into esophagus stopped at level of 4th rib	Diagnosed in 6 hours. Surgery attempted. Only procedure possible was gastrostomy. Died. Autopsy revealed esophageal atresia with tracheoesophageal fistula
C. A Case of Meconium Ileus Associated With Hydramnios							
9	F	Sixth month, with rupture of membranes, discharge of fluid to time of delivery	Unknown	Distended abdomen with epigastric mass	Negative	Accumulation of gas in stomach, duodenum, and proximal jejunum. Scattered air bubbles in small bowel. None in colon. Calcification within dilated segments	Diagnosed meconium ileus with obstruction in 2 hours. Confirmed at surgery. Survived newborn period
D. Two Cases of Fetal Aphagia Associated With Hydramnios							
8	F	Fourth month	10,000	Contractions of legs and fingers. Difficulty in opening mouth and in sucking. Fed by nasogastric tube	Not done	None of alimentary tract	Diagnosis: Arthrogryposis multiplex. Left nursery on 12th day against advice, in bad condition. Sucking poorly
11	F	Fifth month	5,000	Inability to suck and to swallow. No vomiting. Fed by nasogastric tube	Not done	None	Diagnosis: Cranial nerve nuclear agenesis. Had to be tube-fed first year of life
E. Two Cases of Intestinal Obstruction in the Newborn Infant Not Associated with Hydramnios							
5	M	None	None	First feeding not vomited. All succeeding feedings vomited. Marked abdominal peristaltic waves	Negative	Dilated stomach and duodenum in "hourglass" configuration. Gas seen below this. Barium would not pass dilated area	At surgery a mass of adhesions were found involving duodenum. Diagnosis: Duodenal stenosis. Gastrojejunostomy. Survived
12	M	None	None	Mongolism. Vomiting began at 48 hours. Marked abdominal peristalsis and distention	Negative	Dilated stomach and duodenum with fluid levels. Gas seen throughout entire bowel	At surgery annular pancreas found. Gastrojejunostomy. Lived eight days after surgery

in its advanced stages. The mortality in neonatal obstruction is roughly directly proportional to the promptness of diagnosis made within the first two days of life. Thereafter the mortality rises sharply, with rare survival after a week. Thus a need for "aggressive suspicion" has been justly called for by the surgeons,[8] and a contribution can be made by the physician responsible for the newborn infant if the significance of hydramnios is understood.

were of this variety (Table I, *A*). If a newborn infant vomits even before the administration of oral fluids, and subsequently the first few feedings, and particularly if the vomitus contains blood or green bile pigment, the question should be raised as to whether or not the infant's mother had hydramnios. If the question is answered in the affirmative, an x-ray air-bubble study of the abdomen should be made (Fig. 1) and a Farber test[5] done. If these four diagnostic criteria are pres-

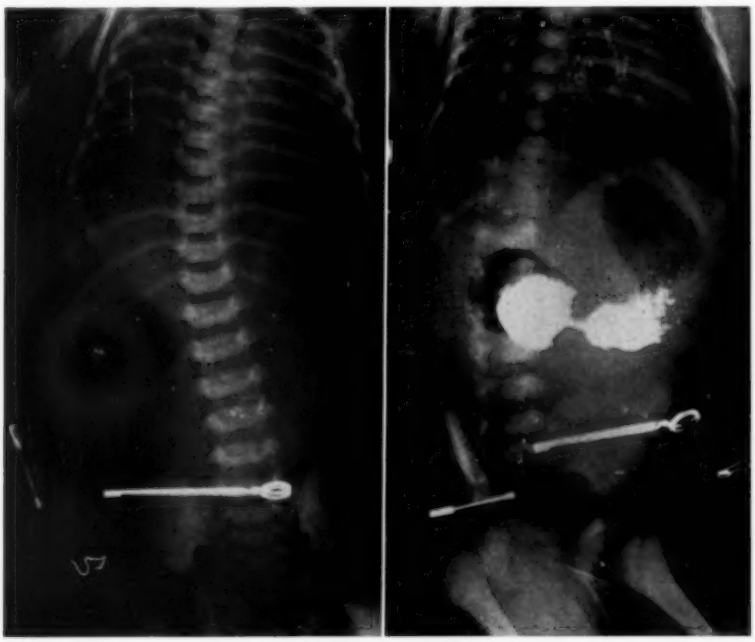

Fig. 1.—Atresia of duodenum with dilatation of proximal duodenum and stomach. "Hourglass" appearance due to normal caliber of intervening pylorus. No air or Lipiodol in bowel below obstruction. Note aspiration of Lipiodol into lung. Radiopaque substance is not necessary for diagnosis. Barium is dangerous. Mother had hydramnios.

The most common entity of the high obstructions of the newborn infant's alimentary tract which hydramnios can alert is that of duodenal atresia. Six of the eight high alimentary tract obstructions observed in twelve years

ent, the infant has an obstruction high in the intestinal tract and should be seriously considered a subject for prompt surgical repair. If the problem is recognized for what it is in 24 to 48 hours, a life may be saved.

Such an infant will reach the safety of surgical repair sooner if the previous observations are noted in reverse order. That is, if at delivery the mother is noted to have hydramnios and its diagnostic significance is appreciated, then the infant's vomiting will have significance sooner, the Farber test[5] will be done sooner, the abdominal air-bubble x-ray study will confirm the diagnosis sooner, and surgery will be done under optimum conditions. Indeed "aggressive suspicion" would be furthered by the routine passage of a catheter into the stomach immediately after birth in any infant born of a mother with hydramnios. This procedure would be done to demonstrate a possible esophageal atresia, or excessive stomach contents suggesting high obstruction. The outstanding clinical sign in esophageal atresia is the newborn's regurgitation of excessive thick mucus, and also the immediate vomiting of any fluid swallowed. In some cases with tracheoesophageal fistula the swallowing of any fluid immediately evokes a paroxysmal choking cough.

The next clinical entity where the mother's hydramnios will alert the physician responsible for her infant is that of esophageal obstruction. About 80 per cent of esophageal malformations have a proximal esophageal atresia with distal tracheoesophageal fistula. One of the eight high alimentary tract obstructions in which maternal hydramnios was associated encountered by this observer was of this type (Table I, *B*).

Ingalls and Prindle[9] reported a series of 102 cases of tracheoesophageal fistula in which 20 were associated with maternal hydramnios. In this abnormality the amniotic fluid has access to the absorbing gastrointestinal tract through a fistulous opening, thus hydramnios should not form. It would appear that the fistula is inadequate for this function in about one-fifth of the cases.

Infants who have high intestinal tract obstruction due to meconium ileus have produced hydramnios in their mothers. One of the eight high obstructions of the newborn alimentary tract associated with maternal hydramnios encountered by this observer was of this type (Table I, *C*). Hydramnios should form only in those cases where the pancreatic dysfunction comes on in early intrauterine life producing the inspissated meconium high in the intestinal tract, preventing the absorptive functioning of the remainder of the intestine. In the mother in our case the hydramnios came on suddenly at the sixth month and became so great that the amniotic membranes ruptured, and she continued to leak amniotic fluid copiously until she delivered a 1,770 gram infant at the end of the seventh month of gestation.

A bizarre condition in which hydramnios occurred, seen by this observer, was arthrogryposis multiplex in a newborn in which the function of the temporomandibular joints was involved (Table I, *D*). Thus intrauterine swallowing was impaired, producing hydramnios in the mother. The same mechanism operated in a newborn infant with nuclear agenesis of cranial nerves who therefore had aphagia and had to be tube fed from birth until a year of age, the last time she was observed (Table I, *D*). Her mother had hydramnios.

DISCUSSION

These ten cases observed had one thing in common, inaccessibility of the amniotic fluid to the alimentary tract, either by mechanical obstruction or by aphagia.

The last two cases where the obstruction was aphagia fit into the most classical association with hydramnios, that of anencephalus. In a study[10] of 145 cases of pregnancy complicated by hydramnios, 68 defective infants resulted, of which the highest number, 45, had anencephalus. All through the literature anencephalus leads in the defect associated with hydramnios. An anencephalic fetus has a neurologic defect causing faulty intrauterine swallowing and breathing. This defect is probably worse than that of the infant with the nuclear agenesis previously described. Apparently it produces a hydramnios of a degree that is most easily discerned clinically, judging by its place at the top of the list of defects associated with hydramnios. It brings the swallowing function into its proper perspective in the prevention or production of hydramnios.

The fact that hydramnios occurs in nonobstructive conditions such as cranial nerve agenesis, arthrogryposis multiplex involving the temperomandibular joint, and most commonly in anencephalus seems to point out that to be an effective absorber the fetus must have the amniotic fluid pushed through the first part of the alimentary tract by vigorous swallowing. This also might be inferred from the fact that although a pathway exists into the gastrointestinal tract in the fetus with tracheoesophageal fistula, roughly one of five produce hydramnios in their mothers,[9] probably because the swallowing is not powerful enough to push through the inadequacy of that fistula.

Whether or not the lungs function as an absorptive mechanism is questionable. The work of Davis and Potter[7] clearly demonstrated that the lungs are permeated by amniotic fluid in fetal life, and furthermore that a concentration of thorium occurred presumably by absorption in the lung. However, in all cases of high obstruction of the alimentary tract producing hydramnios access to the lungs was unobstructed, and had absorption been present it would have prevented hydramnios.

There are infants who have obstruction of the intestinal tract in the neonatal period without having produced hydramnios in their mothers. These are stenotic lesions of the upper gastrointestinal tract where even a tiny aperture left in the lumen of the intestine allows for proper amniotic fluid absorption during intrauterine life, but as soon as milk digestion is attempted an obstruction is formed. Two of these have been observed, one an annular pancreas, and the other apparently the result of an intrauterine peritonitis (Table I, *E*). Other conditions which may act this way are agenesis of the myenteric plexus, peritoneal abscess, meconium ileus forming late and involving only the lower bowel, volvulus low in the tract, and imperforate anus.

One might question why all hydramnios is not associated with dysfunction in the absorptive process of the alimentary or respiratory tract of the fetus. That is to ignore the fact that there

is a maternal absorptive process which can also be faulty. An example is the fact that hydramnios is a well-recognized complication of pregnancies of the diabetic, particularly in mothers with poorly controlled diabetes resulting in hyperglycemia. Hoet and Osinski[11] have recently shown that the electrophoretic pattern of the amniotic fluid present in hydramnios in diabetic mothers is more like that of the mother than that of the infant. This implies that maternal protein enters the amniotic cavity through some defect of the membranes and hydramnios is a consequence of the disturbed osmotic equilibrium. It is possible that the high incidence of hydramnios in pregnancies complicated by erythroblastosis and also by toxemia occur by similar fluid imbalance phenomena.

SUMMARY

1. The experience with eight cases of high alimentary tract obstructions associated with hydramnios was used to illustrate the use of hydramnios as a diagnostic signal for the physician responsible for newborn infants to make him "aggressively suspicious" of the possibility of obstruction and thus to get the infant to surgical repair in optimum condition.

2. The experience with two cases of hydramnios associated with fetal aphagia was used to illustrate the need for amniotic fluid to be forced into the absorbing alimentary tract with vigorous swallowing movements.

3. The experience with two cases of intestinal obstruction of the newborn not associated with hydramnios was used to illustrate that there are a variety of congenital defects of the alimentary tract that allow for the fetal absorptive process, but which obstruct in the newborn period when milk digestion is attempted.

4. That there is a maternal as well as a fetal phase to the absorption of amniotic fluid is illustrated by the high association of hydramnios in pregnancies complicated by diabetes, toxemia, and erythroblastosis. This consideration is necessary so that alimentary tract obstruction is not expected or diagnosed in all instances of hydramnios. In this sense, therefore, hydramnios is a signal to investigate the newborn infant, but not necessarily a diagnostic sign of congenital alimentary tract obstruction.

Dr. Emmet B. Bay, Professor of Medicine, University of Chicago, and Medical Editor of the Encyclopedia Brittanica, gave generously of his time in a critique of the clarity of expression.

Sister Mary deLellis, S.S.M., Nursery Supervisor at St. Francis Hospital, Blue Island, Illinois, cooperated generously in the clinical aspect.

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11. Cited from Prindle, R. E., Ingalls, T. H., and Kirkwood, S. B.[10]

ADDENDUM

Since the acceptance of this paper for publication, an excellent one on the same subject has appeared entitled "Hydramnios as an Aid to the Early Diagnosis of Congenital Obstruction of the Alimentary Tract: A Study of the Maternal and Fetal Factors," by James R. Lloyd, M.D., and H. William Clatworthy, Jr., M.D. (Pediatrics **21**: 903, 1958).

Almost a Snake

Feb. 8th.—*Ascaris Lumbricoides of unusual size.*—Dr. Morland, referring to the lumbricus which he had shown to the Society, December 14th, 1857, said that it was a little over *seventeen inches* long and proportionately large. It was a female and, when first seen, the intestinal and genital apparatus were distinctly visible through the integument; after a few days' immersion in diluted alcohol, the skin became opaque. The parasite was brought to Dr. M. whilst attending outpatients at the Central Office of the Boston Dispensary, by the mother of a little girl nine years of age, and who had passed it spontaneously.

Dujardin, quoted by Küchenmeister in his late work (*Manual of Animal and Vegetable Parasites*) states that the male worm averages from four to six inches in length; the female, seven to eleven; and as the extremest length, mentions *eighteen* inches. The specimen, therefore, has, since its exhibition, been distinguished by Dr. Jackson with an appropriate mounting and a place in the Society's Cabinet.

EXTRACT FROM THE RECORDS OF THE BOSTON SOCIETY FOR MEDICAL IMPROVEMENT, THE BOSTON MEDICAL AND SURGICAL JOURNAL, 1858.

SUPRAVENTRICULAR TACHYCARDIA SIMULATING VENTRICULAR PAROXYSMAL TACHYCARDIA IN INFANCY

AGUSTIN CASTELLANOS, M.D., LUIS AZAN, M.D., JOSE M. CALVIÑO, M.D., AND AGUSTIN CASTELLANOS, JR., M.D.
HABANA, CUBA

VENTRICULAR tachycardia is rare in children.[1] Only during diphtheria[2] or as a terminal event in some viral myocarditis is it a frequent finding.[3]

Several years ago, we reported the effects of intravenous procaine amide in the treatment of paroxysmal supraventricular tachycardia in infancy.[4] In one of our patients this drug produced a marked widening of the QRS complexes, which was due to its direct action on intraventricular conduction. The resultant picture was that of a ventricular tachycardia. As it was possible that a prolonged duration of the ventricular complexes could also occur in spontaneous rapid supraventricular rhythms, a search in our files was made for this phenomenon. During the past two years we observed two of such cases, which shall be reported here.

CASE REPORTS

CASE 1.—In the tracings presented in Fig. 1 there existed a normal sinus rhythm with a right bundle branch block. The sinus rate and the P-R interval were within normal limits, but the ventricular complexes measured 0.12 second. The records were obtained from a 5-year-old boy with no evidence of heart disease, during a routine checkup. There was no reference to any previous illness to which the conduction defect could be attributed.

One year after the first visit, the child complained of chest poundings and palpitations, so that again he was submitted to us for treatment. Since physical examination was again negative, we shall consider only the electrocardiographic findings.

Fig. 2 was recorded after carotid sinus and ocular pressure were ineffective. No P waves could be identified, and the QRS complexes had a duration of 0.12 second, also with a right bundle branch block morphology. The rate was 207 per minute. Were it not for Fig. 1, the diagnosis of ventricular paroxysmal tachycardia would have been made. But, as the ventricular deflections were alike on both occasions, the paroxysmal tachycardia could not have arisen in the ventricles and was obviously supraventricular in origin, yet with anomalous spread in the ventricles due to pre-existing organic bundle branch block. The patient received oral digoxin, 2 mg. in two doses, six hours apart, with prompt restoration of normal sinus rhythm.

CASE 2.—The electrocardiograms featured in Figs. 3-6 belonged to a 9-year-old asthmatic girl with no evidence of heart disease. She had presented intermittently, since her early childhood, paroxysms of rapid heart action, which disappeared, either spontaneously or by reflex vagal maneuvers such as carotid or ocular pressure.

From the Departments of Pediatrics and Cardiology, Hospital Municipal de Infancia; and the University of Habana School of Medicine.

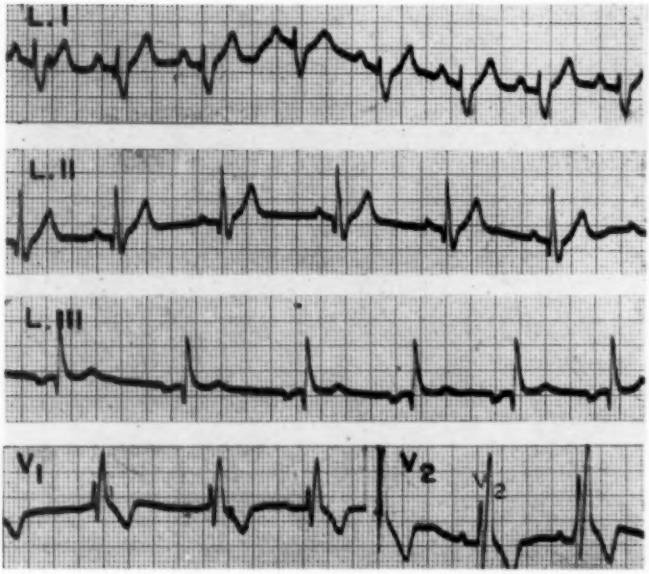

Fig. 1.—Case 1. Normal sinus rhythm and right bundle branch block.

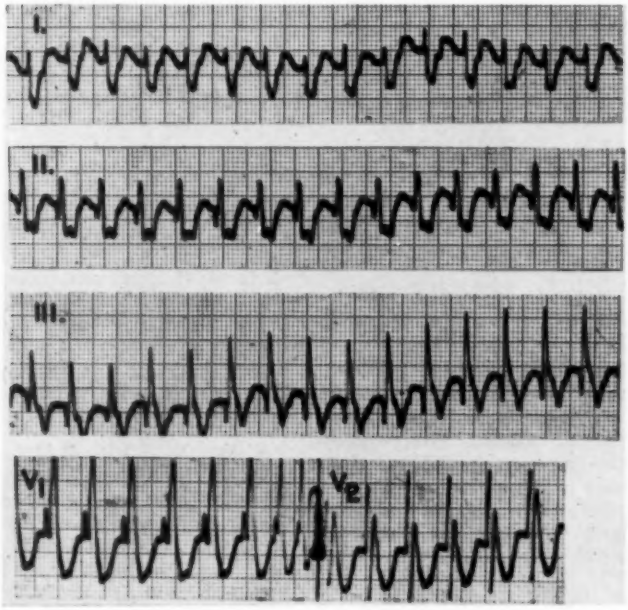

Fig. 2.—Case 1. Supraventricular tachycardia with right bundle branch block imitating ventricular paroxysmal tachycardia.

These paroxysms had a duration which ranged from a few minutes to several hours.

The records in Fig. 3 were taken during one of the attacks. It can be seen that the P waves are absent and that the QRS complexes measured 0.09 second. In Lead VI, the usual RS morphology was not present, and instead there existed an rsR′ pattern which is generally observed in instances of right bundle branch block, leads, always preceding the QRS complexes. Consequently, the diagnosis of an atrial tachycardia was made, its rate being 240 per minute. Accordingly, in this case, the abnormal morphology in Lead VI had to be ascribed, not to an organic bundle branch block, but to a functional, anomalous spread of the atrial impulses in the ventricles, that is, to the aberrant ventricular conduction produced by the high atrial rate.

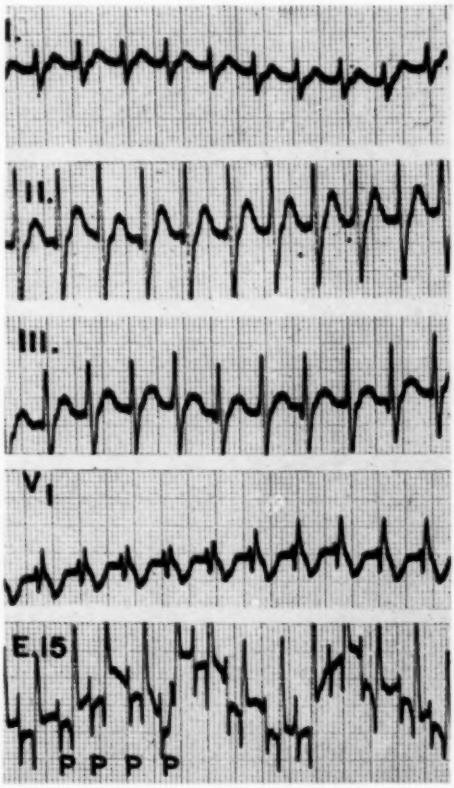

Fig. 3.

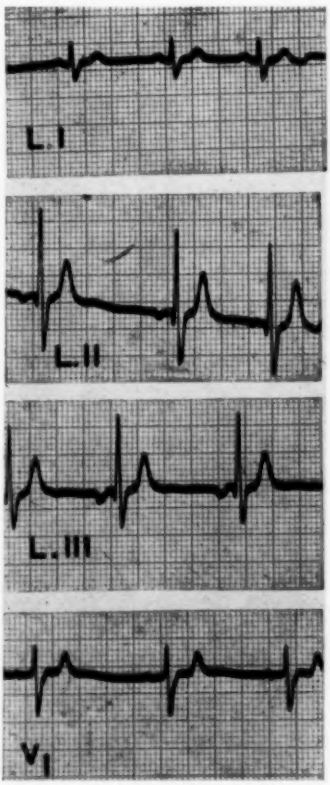

Fig. 4.

Fig. 3.—Case 2. Atrial tachycardia with aberrant ventricular conduction. The correct diagnosis is definitely established by the inspection of the esophageal leads, where the P waves are clearly outlined.

Fig. 4.—Case 2. "Upper" A-V nodal rhythm.

so that a ventricular tachycardia was considered. Nevertheless, the P waves were clearly outlined in the esophageal

Fig. 4 was recorded immediately after the tachycardia ended. Inverted P waves were present in Leads II and

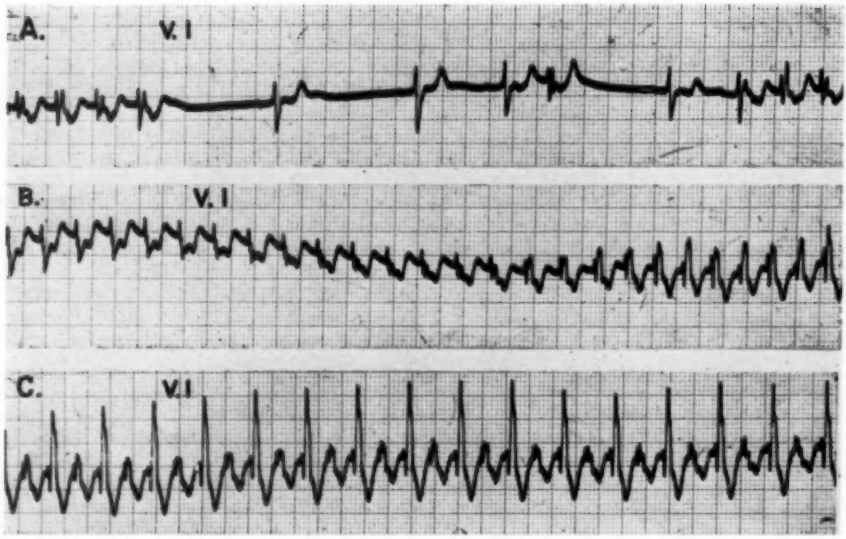

Fig. 5.—Case 2. Repetitive atrial paroxysmal tachycardia. Note the different morphologies of the ventricular complexes due to various degrees of aberrant ventricular conduction.

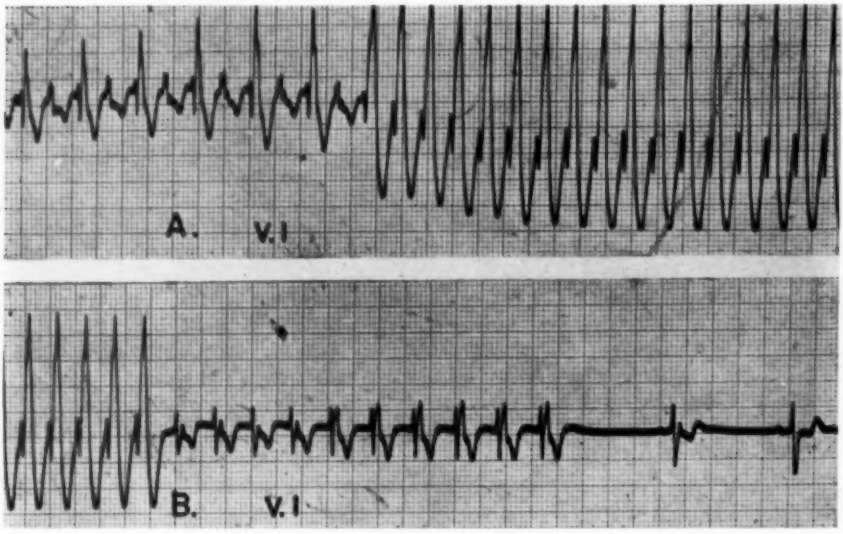

Fig. 6.—Case 2. Atrial tachycardia with marked increase in aberration due to an increase of the atrial rate. The widened QRS complexes simulate ventricular paroxysmal tachycardia. (Discussed in text.)

III, as generally happens in passive nodal rhythms. It is to be noted that Lead VI showed a normal RS morphology. In our experience a prolonged posttachycardial absence of sinus rhythm is unusual in children except when dealing with the repetitive variety of tachycardia described by Parkinson and Papp.[5] Thus, this possibility was considered, and was confirmed by the following tracing.

At the beginning of Fig. 5, *A*, four complexes of the tachycardia were observed preceding three sinus beats, the last of which was followed by an extrasystole with similar morphology to the ones seen during the tachycardia. In *B* (Lead VI), ventricular complexes of varying forms were observed, obviously due to unusual kinds of aberrant ventricular conduction produced by slight changes in the atrial rate. Furthermore, in *C*, the aberration increased alternatively from beat to beat, that is, an rsR′ pattern of shorter duration alternated with one of longer duration. The rate was 250 per minute.

In Fig. 6, *A*, the atrial center speeded up (thirteenth complex) and discharged at a rate of 260 per minute, so that the aberration increased (the QRS complexes were wider that before) and the resulting image was that of a typical ventricular tachycardia.

Finally, at the beginning of Fig. 6, *B*, the same complexes were seen, but when the rate suddenly dropped to 210 per minute (exactly at the top of the letter *B*), aberration again decreased, until the sinus node took over (last two ventricular deflections). The normal beats had the RS morphology which corresponded to the child's age. Although in this patient the prevention of recurrences of this arrhythmia was difficult, we employed, as a trial, oral digoxin (0.5 mg. daily, in two divided doses). To date the results have been encouraging, and the paroxysms have been reduced considerably.

COMMENT

Recently (in adult electrocardiography), Langendorf[6] has emphasized that all tachycardias with prolonged QRS duration are not necessarily of ventricular origin. Possible explanations were analyzed by this author. Undoubtly, these possibilities are more evident in children, where ventricular paroxysmal tachycardia is so infrequent that such a tentative interpretation should immediately raise the doubt as to whether or not one is really dealing with a ventricular tachycardia.[7]

In Case 1, organic pre-existing right bundle branch block was responsible for the prolonged QRS complexes. On the contrary, in Case 2, no organic lesions of the bundle branches were present, and, instead, there occurred a not unusual phenomenon, namely, aberration of an atrial impulse. This term was defined by Sir Thomas Lewis as the "abnormal distribution of a supraventricular impulse in the ventricles."[8] He referred to cases where there existed no anatomic lesions in the bundle branches, when its cause is nearly always an abnormal prolongation of the refractory period of the A-V conducting tissues, mainly of the right branch. This explains why about 88 per cent of the aberrant beats have a right bundle branch block morphology.[9] Aberrant ventricular conduction is generally present at high rates, and, as a rule, the more rapid the rate, the more marked the aberration.

Case 2 also presented evidence of repetitive paroxysmal tachycardia, which is characterized by "recurrent short runs of auricular, nodal or ventricular extrasystoles, and of runs of paroxysmal tachycardia almost constantly present for months or years."[5] For instance, a nodal rhythm existed in Fig. 4, atrial extrasystoles in Fig. 5,

and atrial tachycardia in Figs. 3, 5, and 6. Thus, these disorders of rhythm constitute a definite electrocardiographic entity. From the inspection of the illustrations mentioned above, it is evident that long tracings are very useful when dealing with patients with these arrhythmias.

The two children in this report, with supraventricular tachycardias, had the common feature of presenting prolonged QRS complexes, a characteristic which is ascribed mainly to ventricular paroxysmal tachycardia. Similarly, some patients with the Wolff-Parkinson-White syndrome may occasionally exhibit certain atrial disrhythmias which can also simulate ventricular paroxysmal tachycardia.[10]

Some authors have considered that all supraventricular tachycardias have a regular rate, in sharp contrast with the generally irregular ventricular ones.[7] However, experiments performed by Scherf and associates[12] have revealed that the inverse is also frequent; hence this feature cannot be considered per se of diagnostic importance (Figs. 5 and 6).

Similarly, this author showed that variations in rate are not to be attributed to modifications in the path of a circulating wave, that is, to circus movement, for they can be produced simply by an irregular discharge of an ectopic focus, due to various conditions. Furthermore, in another report from our department, the presence of a 2:1 exit block was certainly diagnosed during an atrial tachycardia, and as this condition is exclusive of automatic centers, it was firmly and definitely established that some of the tachycardias observed in man are produced by the rapid activity of an ectopic automatic center.[13]

We want to emphasize that every attempt should be made to clarify the genesis of the arrhythmia, for it is important for prognosis as well as for treatment. Theoretically, digitalis is the drug of choice in supraventricular tachycardias, but in the ventricular ones quinidine or procaine amide should be tried first.[7]

Esophageal leads have been found useful in the diagnosis of complex disorders of rhythm.[11] Nevertheless, they have been neglected in children, mainly in infants, on account of obvious technical difficulties. In the older children they can be used (as shown in Fig. 4) as an aid in the establishment of the correct electrocardiographic interpretation, which in Case 2 was possible only by the inspection of such leads.

SUMMARY

Two examples of supraventricular tachycardias with prolonged QRS complexes were presented. This prolongation was produced in one case by the previous existence of an organic bundle branch block and, in the other case, by aberrant ventricular conduction of the atrial impulses, due to the rapid heart rate. The importance of the correct diagnosis was stressed, especially when prognosis and treatment were to be considered.

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Casein at Fault

It cannot then be supposed that milk adapted to the stomach of a calf would suit that of a new-born child. Common observation agrees with chemical analysis in declaring that there is too much casein in the milk of a cow to be tolerated by the child. This is a well-known fact, and every one waters the milk. But "how much water must be used?" and "will watering do no harm?" are questions to be answered only by careful study of the milk and close observation of its effects upon the child.

Cow's milk contains nearly three times as much casein as human milk, but less than twice as much butter. In cow's milk, the butter is to the casein as 100 to 105; in human milk, as 100 to 70. If then, by dilution, we reduce the butter to 20.76, we shall have 21.92 of casein, or 50 per cent. more than in human milk. With such an excess of casein, we cannot hope to succeed. The stomach of the child cannot digest it, and it will thus pass through the intestinal canal, irritating as it goes. Debilitating diarrhoea and, perhaps, vomiting will occur, and the attempt fail.

CUMMING, WM. HENRY: ON NATURAL AND ARTIFICIAL LACTATION, AM. JOURNAL OF MEDICAL SCIENCES, VOL. 36, 1858.

INFLUENZA ENCEPHALITIS

WILLIAM J. MELLMAN, M.D.
PHILADELPHIA, PA.

THE possibility that a single agent is etiologically responsible for both epidemic influenza and encephalitis has been debated since the turn of the century. The appearance of a new strain of influenza virus causing epidemic disease in 1957 may help resolve this dilemma. The printed evolution of this debate will be reviewed, and suggestive clinical and laboratory evidence that encephalitis indeed may be caused by the influenza virus will be presented.

Osler[1] in 1892 described marked delirium and meningitis as striking features of influenza, and a standard clinical text[2] mentions reports of sleeping sickness with the influenza epidemic of 1712. Leichtenstern[3] in 1905 presented a comprehensive discussion of the neurological and pathological findings in influenza, stating that the neurological symptoms in influenza were second only to those of the respiratory tract. Among the patients he described was a group with "acute focal hemorrhagic encephalitis." This disease occurred with an acute onset, usually at the beginning or height of the influenza attack, manifested by apoplexy, high fever, delirium, coma, and convulsions. He described complete recovery in some of these patients. Interpretation of these earlier writings should be influenced by the fact that the influenza bacillus was popularly considered at that time to be the cause of epidemic influenza.

The striking coincidence of the world-wide epidemics of influenza and encephalitis between 1917 and 1919 stimulated considerable discussion of a possible causal interrelationship. In 1934, Thomson and Thomson[4] reviewed 4,500 articles relating to the complications of influenza, and cited many case reports of encephalitis in association with influenza epidemics. They presented these hypotheses: (1) Encephalitis as it occurs in influenza epidemics is due to a neurotropic influenza virus. (2) The influenza virus predisposes the individual to a second agent producing the encephalitis. (3) The two diseases are completely unrelated and their association is purely coincidental. They concluded that the resolution of this controversy depended on elucidation of the etiological factors involved.

Epidemiological studies of multiple outbreaks of influenza throughout the world between 1917 and 1932 were reported by Hurst[5] in 1934, and reviewed by Jordan.[6] Hurst mentioned a report of almost three-quarters of a million cases of influenza in the United States Army during 1918-1919 without a single case of encephalitis among the secondary diagnoses listed. A careful analysis of incidence curves of

From the Department of Pediatrics, Hospital of the University of Pennsylvania.

encephalitis and influenza in South Carolina from 1925-1929 revealed a complete dissociation. They concluded, therefore, that there was no correlation between the two diseases.

It is interesting to note that a United States Public Health Service report in 1929 (quoted by Hurst[5]) compared the epidemics of 1888 and 1918-1919, stating that the earlier epidemic was marked by neurological symptoms while the latter was predominantly one of catarrh. Once the question of possible strain specificity as a factor in the clinical manifestations of a particular epidemic of influenza was entertained, it became obvious that the resolution of the problem required an approach other than an epidemiological one.

In 1937 Neal and Wilcox[7] proposed the use of the newly available technique of serological diagnosis. They studied sixteen cases of "grippe" or "influenza" with subsequent neurological symptoms, and found that only one of these patients had a demonstrable rise of neutralizing antibodies to influenza virus in the convalescent serum. They, too, concluded that there was no etiological relationship between influenza and encephalitis. Aldrich[8] reported 1,146 cases of "grippe" diagnosed in pediatric practice and noted only two cases of encephalitis among the complications listed. In 1945 Broun and associates[9] reported encephalitis in a 51-year-old patient who developed a rise in influenza A antibody titer sixteen days after onset of the illness; in addition, a virus isolated from the spinal fluid was incompletely proved to be that of influenza. In 1953 Marquézy[10] described sixteen children in France aged 7 months to 9 years who developed a rise in hemagglutination inhibition antibody titers. Ten of these children had encephalitis with coma and convulsions, and several were autopsied with pathological findings similar to those described by Leichtenstern some years before. In all but one of the sixteen children, the predominant antibody rise was in influenza A prime strain. The authors concluded that certain strains of influenza virus demonstrate neurotropism.

The current epidemic of Asian influenza has provided a new stimulus to examine the relationship of influenza to encephalitis. In the initial reports of recent epidemic influenza outbreaks, descriptions appeared suggesting encephalitic complications. Unfortunately, most of these have lacked laboratory confirmation. Guthrie[11] described 5 of 1,429 cases in Kuwait who presented themselves with headache and neck rigidity of 48 hours' duration. In Kuala Lumpur, Turner and Helliwell[12] stated, "Several young children have shown meningismus and this has been noted in three fatal cases which had terminal convulsions and coma. These cases were not proved virologically." Giles and Shuttleworth[13] in a report of 46 influenza deaths, described the findings in two patients diagnosed ante mortem as acute encephalitis. Necropsy revealed intense congestion and edema without microscopic evidence of encephalitis. Dubowitz[14] has recently described two cases of encephalitis occurring in South Africa with serological evidence of influenza A infection.

During the Asian influenza epidemic in the fall of 1957, two children were admitted to the pediatric service of the Hospital of the University of

Pennsylvania with the clinical diagnosis of encephalitis. Serological studies in these children demonstrated significant titers of antibody to the Asian strain of influenza virus.

CASE REPORTS

C. E., an 8-year-old girl of Oriental extraction, was well until four days prior to hospitalization on Oct. 23, 1957, when she developed fever of 102° F. and sore throat. She seemed to improve over the next 48 hours, but then developed a recurrence of fever, cough, and vomiting. These symptoms persisted along with lethargy progressing to stupor on the day of admission. There was no history of influenza vaccination.

On admission she was responsive only to painful stimuli and at times was delirious. There were no meningismus or localizing neurological signs. Laboratory studies revealed normal blood count, urinalysis, blood sugar, and serum electrolytes. A lumbar puncture revealed: cells none, protein 33 mg. per cent, glucose 65 mg. per cent, and no growth on bacterial culture.

Following the lumbar puncture the patient became more responsive for a short time. She retained oral fluids for the first 24 hours, but then lapsed into a state of unresponsiveness during which time she developed bilateral Babinski signs and extensor spasm in the lower extremities. Starting on the third day, hydrocortisone 50 mg. was given intramuscularly every 8 hours for 3 days. Within 12 hours after starting hydrocortisone she became more responsive, and in the next 24 hours became alert. By the eighth day she was considered well and was discharged.

She was seen in follow-up clinic 3 weeks and 3 months later. On the first visit she complained of lethargy and labile emotions, but appeared well to the examiner. On the second return visit she was considered completely well. Neurological examination was normal and a psychological examination reported superior intelligence with no evidence of organic disturbance.

The following viral antibody studies were reported:

Influenza complement fixing titers (Table I).

TABLE I

	Soluble A	*Strain Specific Asian**
10/25/57 (6 days after onset)	1:256+	<1:8
11/22/57 (1 month after onset)	1:32	1:128
1/24/58 (3 months after onset)	1:48	1:32

*Method described by Lief and associates.[15]

Negative titers to lymphocytic choriomeningitis, mumps, and poliomyelitis.

J. H., a 5-year-old Negro boy, was hospitalized on Nov. 15, 1957, with an 8-day history of fever and headache. Five days prior to admission he developed abdominal pain and vomiting which recurred until the time of admission, although the fever seemed to remit. On the day of admission he developed fever to 104° F. and a stiff neck. There was no history of influenza vaccination.

On admission he appeared acutely ill with marked nuchal rigidity, dilated pupils, and mild pharyngeal congestion. There was generalized tenderness and guarding of the abdomen. Laboratory studies revealed a normal blood count and urinalysis. A lumbar puncture showed a pressure of 240 mm. water, 3 white cells per cubic millimeter, protein 18 mg. per cent, glucose 53 mg. per cent, chloride 121 mg. per cent, and no growth on bacterial culture.

Immediately following the lumbar puncture, the patient became more alert and less rigid but, within the next few hours, again developed neck rigidity and lethargy. Over the next

72 hours his sensorium varied from complete responsiveness to stupor. His meningismus also was remitting; temperature intermittently rose to 102° to 105° F., and gradually subsided over the next five days. During this period, multiple blood, stool, and urine cultures all failed to grow any significant pathogens. There was no evidence, as revealed by serodiagnosis, of infectious mononucleosis (heterophile antibody assay), tularemia, salmonella or shigella infection, or of a rickettsiosis (Weil-Felix reaction). He became afebrile on the seventh hospital day but was kept under observation for 15 days, at which time he was discharged.

He was seen in a follow-up clinic 2½ months later, at which time he was completely asymptomatic and had no abnormal neurological findings of his disease. A psychological examination performed 3 months after the acute illness reported average intelligence with no evidence of organic pathology.

The following viral antibody studies were reported:

Influenza complement fixing titers (Table II).

TABLE II

	Soluble A	*Strain Specific Asian**
11/15/57 (8 days after onset)	1:32	1:48
11/26/57 (20 days after onset)	1:32	1:32
2/ 3/58 (3 months after onset)	1:16	1:4

*Method described by Lief and associates.[15]

Negative titers to influenza B, Q fever, psittacosis-lymphogranuloma venereum group, adenovirus, lymphocytic choriomeningitis, mumps, and poliomyelitis.

DISCUSSION

The development of significant antibody titers to influenza virus in two patients with clinical encephalitis, occurring during the recent Asian influenza epidemic, lends further credence to the hypothesis that at least the Asian strain of influenza virus may be etiologically responsible for neurological disease. Although the available statistics are incomplete, a significant number of encephalitides have occurred in the United States during the recent epidemic, many with demonstrated rises in Asian virus antibody titer. Between September and December, 1957, twenty-one cases of influenza encephalitis were reported to the United States Public Health Service.[16] At least two successful virus isolations have been made from the brains of fatal cases of influenza.[17]

The fact that a group of patients with clinical encephalitis has a demonstrable rise in influenza antibody titer during an influenza epidemic may be only coincidental, since the infectivity rate of influenza virus may be very high in a susceptible population. In a recent study,[18] 78 per cent of an unvaccinated group of human volunteers developed serological influenza infection when challenged with Asian influenza virus. A larger number of isolations of influenza virus from the brain or spinal fluid will be needed as confirmatory evidence that the virus can involve the central nervous system in man. It is further possible that along with the influenza virus these patients may be infected with a second agent that is still unidentifiable by current techniques.

Attempts to demonstrate neurotropism of influenza virus in experimental animals has met with varying results. Stuart-Harris[19] was able to produce

fatal nervous disease in mice by intracerebral injection of an adapted WS strain of influenza virus. Francis and Moore[20] confirmed this observation and showed that the Melbourne strain could also be adapted to produce neurotropism in mice. To date these are the only two strains of influenza virus that will both propagate in the mouse brain and produce neurological disease. Henle and Henle[21] have shown that a number of influenza A and B strains are toxic to the central nervous system when injected intracerebrally into several laboratory animals, but they were unable to produce multiplication of these viruses in brain tissue. However, they could not separate the toxic factor from the active virus particle by various inactivation methods and could neutralize the toxic properties of the virus with type specific antisera. The significance of this toxicity in human infection is still undetermined.

Should influenza virus indeed be responsible for encephalitis during epidemics, late sequelae, such as basal ganglia disease, become a real concern, and will be determined after the long-term follow-up of patients proved by laboratory means to have been infected with influenza virus.

SUMMARY

Acute encephalitis has been reported in association with epidemics of influenza. The incidence of this association has varied from epidemic to epidemic over many years.

Encephalitis has occurred as a complication during the recent epidemic of Asian influenza. Evidence from the virus laboratory supports this thesis. This evidence was not available in major epidemics up to the present time.

The clinical description of two recent cases of influenza encephalitis is reported.

I wish to acknowledge with thanks the help of the following: Dr. Lewis A. Barness, Acting Chief of Pediatrics, Hospital of the University of Pennsylvania; Dr. Florence S. Lief, Virus Diagnostic Laboratory, Children's Hospital of Philadelphia; Dr. Keith E. Jensen and Dr. Frederick Dunn, Communicable Disease Center, Atlanta, Georgia; and Dr. Charles Wenar, Child Psychologist, Hospital of the University of Pennsylvania.

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The Abrahamic Covenant

The sensation created in Austria by the refusal of a Jewish physician to have his son circumcised, on the score of the dangerous character of the operation, has given rise to a thorough scientific discussion of the subject in a Viennese medical paper, entitled *Austrian Gazette of Practical Medicine*, in which the following results are arrived at:—1. That circumcision, as a medical operation, presents no kind of danger whatever; that if it should be followed by any untoward consequence, it is owing to the unskilfulness of the operation. 2. That the mortality amongst Jewish children is not greater than that amongst the Gentile children of the same class. 3. That circumcision exercises no unfavorable influence whatever upon the Jewish constitution. 4. That it protects from various physical evils, which it either altogether averts or greatly mitigates.—*Abridged from Lien D'Israel.*

As reported in the Boston Medical and Surgical Journal, May 27, 1858.

STUDIES ON THE pH OF THE RESPIRATORY TRACT

I. Endotracheal Aspirate of the Healthy Newborn Infants

Sydney Jacobs, M.D.,* and Sol M. Papperman, M.S., M.D.,**
New Orleans, La.

Much attention has been directed traditionally to the type of organism causing tracheobronchial and pulmonary disease and little to the tissue change itself. The importance of host factors in determining the type of disease and even the outcome of the illness was given emphasis by the recent work of Selye[1] who, in 1951, administered excessive amounts of ACTH and cortisone to rats and produced pulmonary abscesses with organisms usually regarded as nonpathogenic. Kass and co-workers,[2] Robinson and Smith,[3] as well as Schwartzman and Aronson[4] demonstrated in similar studies that, when infection results in fatality or prolonged morbidity, decreased host resistance may be responsible more often than generally appreciated.

To study this problem in human beings is not easy, and to draw conclusions from animal experimentation is not always warranted. Clinicians believe that "decreased resistance" frequently modifies the outcome of infectious disease but do not know how to measure this phenomenon quantitatively or to be certain when it exists. In an effort to throw some light on this puzzling phenomenon, a series of studies was projected. Measurement of the pH of respiratory tract secretions was selected for portraying tissue changes produced by disease, notably infection, further modified by the effects of powerful medicaments such as the antibiotics and the corticosteroids.

The pH of secretions of the respiratory tract may reflect tissue changes occurring during the course of various diseases, particularly those produced by infections. In a unique investigation, Steinman[5] inserted a specially constructed electrode through a bronchoscope and noted in healthy adults the pH of the tracheal wall to average 5.9—6.6 and of the carina to average 5.8—6.4. Purulent secretions, irrespective of the type of organism producing the disease, caused the pH to rise to 7.1—7.7. The presence of the electrode, itself, he believed to produce sufficient irritation to affect significantly the intravital determinations.

To learn whether the pH of a given specimen is of importance clinically and whether it indicates significant tissue change, it must be known whether it varies materially from the

From the Respiratory Disease Laboratory of the Touro Infirmary at New Orleans and the Department of Medicine of the Tulane University School of Medicine.

This study was supported by a grant from the Jacob M. Aron Research Fund of Touro Infirmary.

*Chief of Medicine, Touro Infirmary.

**Jacob M. Aron Research Fellow, Touro Infirmary.

norm. Inasmuch as normal standards have not been established and since so little is known of the microbiological flora of the respiratory tract in infants (and the possibility that this may influence the pH of secretions), the first set of determinations concerned newborn infants. Smith[6] recently commented on our lack of knowledge of the establishment of the flora in the respiratory tract of the newborn infants and how the first organisms gain entrance.

METHODS AND MATERIALS

Endotracheal aspirations were performed at birth and again 24 hours later on 43 normal healthy newborn babies delivered on the Obstetrical Service of the Touro Infirmary. Three of these were by cesarean section, one by breech presentation, the remainder by vertex presentations. Immediately following delivery of the baby, sterile swabs were made of the maternal vaginal secretions, and the material so obtained was cultured. Endotracheal aspiration was performed by one of three obstetrical residents specially trained in this technique. Wearing sterile gloves without tale, the operator moistened the tip of a De Lee catheter with sterile water, crooked it slightly and guided it into the trachea with the index finger, being careful not to occlude the catheter tip with the finger. During the procedure, the infant's head was hyperextended by a towel roll under the neck. The De Lee glass trap was then fitted into position for removal of secretions by oral suction. The specimen thus obtained was expelled from the glass trap by positive pressure of a 50 ml. syringe (or by mouth) into a sterile glass bacteriological culture tube of a low alkali content. An aliquot of this was then tested for pH on the Beckman pH meter Model G, using the Beckman One Drop Electrode Assembly (Beckman 290-82) and the remainder cultured on the following media (Difco base): Blood agar, Levine eosin-methylene blue agar, nutrient agar, antibiotic No. 2 media, thioglycollate broth, thiol medium and —later in the series—Sabouraud's medium. The same media were used in preparation of cultures from vaginal secretions. Sabouraud's media cultures were allowed to remain as long as 10 days at room temperature whereas the other cultures were incubated at 37° C. for 24 hours, the media examined for growth, and then re-incubated 24 hours. Whenever signs of growth were noted, the material was examined by Gram stain and then identified by the usual cultural characteristics, morphology on staining and biochemical activity.

The catheters and glass traps were prepared by washing in a commercial detergent (Evenflo) and rinsing in tap water until clean. The catheters were successively rinsed repeatedly in distilled water, immersed in 1:2,000 solution of mercury bichloride 20 minutes, rinsed in sterile distilled water, heat dried, and placed in a sterile enameled pan until ready for use. The glass traps were autoclaved at 15 pounds pressure for 20 minutes, heat dried, and placed in sterile enameled pans along with the De Lee catheters. All instruments were handled by sterile forceps.

RESULTS

The mean pH of neonatal endotracheal aspirate was 7.6; 24 hours later it averaged 7.45 (Fig. 1). This

mean difference of 0.31 pH is statistically significant and represents an approximately threefold increase in hydrogen ion concentration. In only 3 of the 43 infants, did the 24-hour aspirate reflect a pH higher than at birth. The mean pH at birth was 7.76 whether or not the endotracheal aspirate contained organisms which grew on culture. At 24 hours the pH was 7.48 for specimens containing culturable organisms and 7.45 for "sterile" specimens; this is not statistically significant.

hour examination. Of the 3 babies delivered by hysterotomy, only one had a positive culture and this at birth. Only once was the same organism (*E. coli*) isolated from the endotracheal aspirate and the vaginal secretion.

A variety of organisms was obtained from the neonatal and the 24-hour aspirates: *Pseudomonas aeruginosa*, alpha streptococcus, *Escherichia coli*, *Neisseria flavescens*, *Bacillus subtilis*, diptheroids, *Diplococcus pneumoniae* (rough). From the 7 cultures of 24-

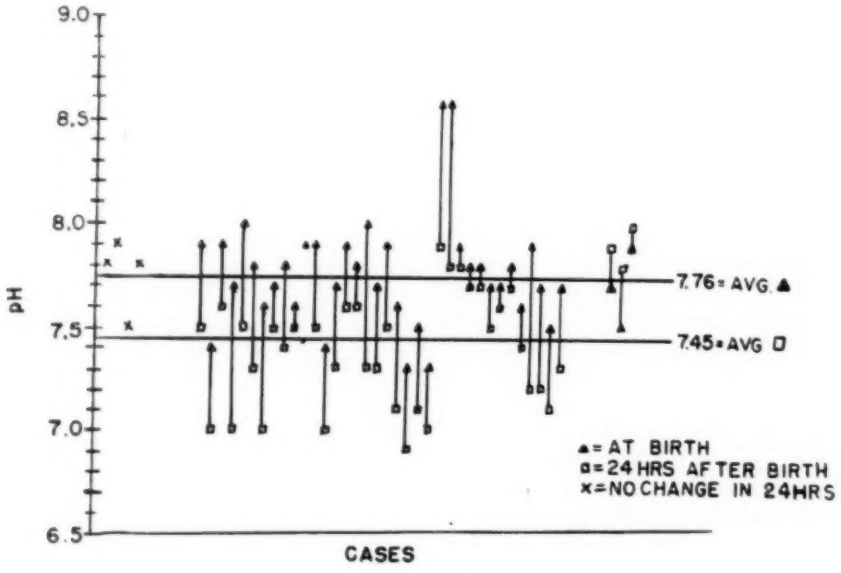

Fig. 1.—pH of endotracheal aspirate.

As indicated in Table I, 31 preparations of the neonatal endotracheal aspirate were sterile; only 12 (27.9 per cent) contained organisms. Similarly, 7 (16.6 per cent) of the 24-hour cultures had demonstrable growths. For only 2 infants were positive cultures obtained both neonatally and at the 24-hour specimens only gram-positive organisms were grown, although one specimen contained both gram-positive and gram-negative organisms. Of the 35 vaginal cultures prepared at birth, organisms (*Proteus vulgaris, Aerobacter aerogenes, Esch. coli* and monilia species) grew from only 8.

TABLE I. pH AND ECOLOGY OF ENDOTRACHEAL ASPIRATES

NEONATALLY			POSTNATALLY		
		AVERAGE pH	AVERAGE pH		
Specimens yielding gram-positive organisms	7	7.84	7.48	7	Specimens yielding gram-positive organisms
Specimens yielding gram-negative organisms	5	7.64	7.40	1*	Specimens yielding gram-negative organisms
Specimens yielding no growth	31	7.76	7.46	35	Specimens yielding no growth

*One culture contained a gram-positive and a gram-negative organism.

COMMENT

The statistically significant drop in pH of endotracheal aspirate observed within 24 hours after birth seems to be unaffected by the type of feeding offered the infant (usually only glucose solutions), the presence of organisms in the aspirate—or even the type of organisms or the presence of recoverable organisms from the maternal vaginal secretions. The paucity of organisms isolated from the maternal vaginal secretions was impressive. Relative sterility of endotracheal aspirate neonatally as well as 24 hours later deserves attention, as does the fact that the first organisms to become established in the respiratory tract were usually gram-positive cocci. Evidently some factor or factors other than bacteria must account for the changes in pH during the first 24 hours of life.

Since this portion of the investigation was primarily elaboration of a technique, all procedures were repeatedly reviewed to discover errors which could significantly affect the results and impair validity of observations. Three different physicians obtained the neonatal specimens while a single investigator (S. P.) obtained the 24-hour specimens, examined them for pH, and conducted all microbiological studies. The relative uniformity of results suggests that the measurement of pH or outcome of bacteriological investigations seems not to have been influenced by the fact that not all specimens were obtained by a single researcher. The occasional inevitable delay in transmitting specimens to the laboratory for examination again could conceivably have permitted loss of carbon dioxide from the obtained secretion and affected the pH; if this does occur, presumably it effected an almost constant loss because the pH determinations were so uniform. Wherever duplicate determinations could be performed, the observations were almost identical. These specimens removed from the glass trap by oral expiratory pressures seemed not to differ in pH from those expelled by air forced through a 50 ml. sterile glass syringe.

Further studies of adults are projected to utilize Steinman's method of endobronchial electrode placement to determine tissue pH of healthy and of diseased subjects and to learn what changes, if any, occur in pH of secretions as these pass along the course of the respiratory tract.

SUMMARY

Preliminary studies on the endotracheal aspirate of 43 normal healthy newly born infants, obtained neonatally and 24 hours later using the De Lee catheter and glass trap, indicate that the pH of these secretions at birth

averages 7.76, dropping to 7.45 by 24 hours later; these changes are statistically significant and are not influenced by whatever organisms happen to grow in the secretions, or by organisms present in the vagina of the mother. Bacteria are the exception, not the rule, and appear not to be derived from the maternal vagina. The secretions tended to be slightly more copious at birth than 24 hours later, possibly because of aspiration in utero.

We are grateful to Dr. Max Rosenberg (Chief Obstetrical Resident), Dr. Edward Serrano and Dr. Ralph Lupin (Obstetrical Residents) for their co-operation and persistence in obtaining specimens despite the multiplicity of their duties; to Dr. Walter E. Levy (Chief of Obstetrics) and Dr. J. D. Russ (Chief of Pediatrics) for their unfailing kindness and help in making available to us the clinical facilities of Touro Infirmary, and to Dr. Hulda Bancroft, Professor of Biostatistics, Tulane University School of Medicine, for assistance in interpretation of data. We are particularly indebted to Dr. Morris Shaffer (Chairman of the Department of Microbiology, Tulane University School of Medicine) for the encouragement and guidance which made this investigation possible.

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ROCKY MOUNTAIN SPOTTED FEVER IN CHILDREN

CONSTANTIN MISSIRLIU, M.D., MARIE F. MISSIRLIU, M.D., AND
JAMES N. ETTELDORF, M.D.
MEMPHIS, TENN.

INITIALLY described and recognized in the Rocky Mountain states, Rocky Mountain spotted fever (tick typhus) has recently been shown to be endemic in all sections of the United States. A number of articles dealing with this disease have appeared in the literature, and an exhaustive review was recently published by Cowley and Wheeler.[1] Nevertheless, reports in children have been few or limited to isolated cases. No major series of cases in children has been reported upon in the past ten years. A study of twenty-five cases in children by Peterson and associates[2] in 1947 still constitutes an authoritative study of the clinical manifestations of the disease. None of their patients received specific antibiotic therapy, para-aminobenzoic acid being the only therapeutic agent available at the time. In 1948, Pincoffs and associates[3] and Ross and his co-workers[4] showed the remarkable and parallel action of chloramphenicol and oxytetracycline in Rocky Mountain spotted fever in adults. The effectiveness of these drugs in children with the disease was subsequently shown.[5, 6] Further reports showed chlortetracycline and tetracycline[7, 8] to be effective antirickettsial agents in adults.

The present series of eighteen proved and two probable cases was observed during a twelve-year period, from 1946 to 1958. These cases illustrate not only the clinical features of the disease but also the results obtained with several of these therapeutic agents in the pediatric age group.

CLINICAL FEATURES

The most salient and constant feature of the disease was a maculopapular rash appearing over the extremities, spreading centripetally to the trunk and also involving the palms and soles. However, it should be kept in mind that Rocky Mountain spotted fever without a rash has been reported in children.[10] The chief reason for hospitalization in all our patients was the presence of a petechial and morbilliform rash which appeared three to ten days after the onset of fever (average, four days). Occasionally, the petechiae became confluent and necrotic (Fig. 1). Skin biopsies were taken in six cases, and in five instances typical lesions of panarteritis were observed.[11]

A high fever was a frequent finding at the time of admission, being absent in only two cases. All patients showed some evidence of central nervous system involvement ranging from restlessness to complete stupor.

From the Division of Pediatrics, University of Tennessee College of Medicine; the Frank T. Tobey Memorial Children's Hospital, City of Memphis Hospitals; and the LeBonheur Children's Hospital.

Intense myalgia and malaise were highly constant complaints.

Less frequent features consisted of (1) edema of the face and puffiness of the eyelids observed in eight cases; (2) moderate enlargement of the spleen in seven cases which was combined with slight hepatomegaly in two cases; (3) nausea and vomiting which occurred in two cases; (4) petechiae of the scrotum which were seen in one patient (Fig. 2).

Fig. 1.

Fig. 2.

Fig. 1.—Note petechial and necrotic aspect of rash on buttocks.
Fig. 2.—Characteristic rash involving soles and accompanied by petechiae of the scrotum.

The diagnosis was considered as very likely on admission in all cases with the exception of one. In this case, the rash was disappearing, and fever was the major symptom. Meningococcemia was the most frequently considered alternate diagnosis. Therefore, lumbar punctures were performed in ten cases on admission. The cerebrospinal fluid showed normal cell counts, protein, and sugar values. Endemic typhus was eliminated in all cases on the basis of the severe clinical course, distribution of the rash, and negative complement fixation reaction.

LABORATORY FINDINGS

Weil-Felix reactions were performed on admission and repeated serially in all cases of this series. Seventeen patients were found to have elevated agglutinin titers for Proteus OX-19 (Table I) at some time during their course. Of thirteen patients admitted before the eighth day of the disease, only four had positive reactions on admission, ranging from 1:80 to 1:320. The reactions eventually became positive between the eighth and fifteenth day after onset of fever. Rising titers were consistently observed, and maximum titers ranging from 1:160 to 1:5,120 were attained in the third week of the disease.

Complement fixation reactions were performed in eight cases of this series and were uniformly positive. Reactions were negative before the fifteenth day of the disease. Maximum titers ranging up to 1:640 were attained in the fourth week of the disease.

One patient, W. A., with persistently negative Proteus OX-19 agglutination reactions had positive complement fixation reactions. Therefore, we felt justified in including in our series patients G. S. and Z. S., in whom complement fixation reactions were not performed and negative agglutination reactions were obtained on the evidence of their typical clinical picture.

Other laboratory findings were (1) moderate leukocytosis, ranging from 7,000 to 12,000 white blood cells per cubic millimeter, with predominant polymorphonuclears (70 to 90 per cent); (2) constant anemia, ranging from 2.5 to 3.5 million red blood cells per cubic millimeter; (3) negative blood and stool cultures (taken to rule out meningococcemia and typhoid fever); (4) negative febrile agglutinations for tularemia, undulant fever, and the Salmonella group (except in individuals having previously received typhoid immunization); (5) low total serum protein level in the 4 to 5 grams per cent range in four patients; (6) low serum chloride values in the 60 to 80 mEq. per liter range in three patients. The latter findings of low chloride values were not associated with vomiting.

COMPLICATIONS

Proteinuria was observed in three cases. In two of these cases, C. D. and W. M., this was associated with microscopic hematuria, granular casts, and an elevation of the serum nonprotein nitrogen. In one of these cases, C. D., a severe acidosis and rapidly fatal hemorrhagic tendency also developed.

Hematemesis was observed in two cases, once in the form of minimal streaks of blood in the patient's vomitus (C. W.), and once as a massive, fulminating hemorrhage (C. D.). In both cases, no clotting defect could

TABLE

PATIENT	AGE (YR.)	DATE (MO. AND YEAR)	RACE AND SEX	HISTORY OF TICK BITE	SPLENIC ENLARGEMENT	ADM. AFTER ONSET (DAYS)	DAYS AFEBRILE AFTER RX
C. H.	7	5-45	WM			7	11
B. K.	10	6-46	WM		+	3	16
C. D.	7	7-46	WF	+	+	11	11 (died)
B. H.	9	7-46	WM			7	8
A. E.	6	7-46	WM		+	8	4
T. B.	7	11-46	WF			6	10
D. S.	8	7-49	WM	+		7	11
C. S.	4	7-49	WM			6	5
L. W.	12	8-49	WF	+		5	4
G. G.	13	6-50	WM	+		5	17
A. G.	3	7-51	WF		+	5	3
W. A.	3	8-51	WM	+		4	4
L. M.	5	5-54	WF			14	4
G. S.	8	6-54	WM			6	3
W. M.	5	9-54	WF			10	14
G. M.	6	6-55	WM	+		5	5
P. T.	5	6-55	WF			15	1
Z. S.	13	8-55	CF			4	4
A. W.	9	7-57	WF	+	+	10	6
C. W.	6	1-58	WM			15	1

I

PROTEUS OX-19 AGGLUTINATION		COMPLEMENT FIXATION				
TITER	DAY OF DISEASE	TITER	DAY OF DISEASE	THERAPY	24-HOUR DOSE	COMPLICATIONS
1:640	18	1:160	23	Sulfa Penicillin	2 Gm. 160,000 units	Edema
1:320	9	1:640	23	Sulfa Penicillin	3 Gm. 160,000 units	
1:320	15			Sulfa Penicillin	3.5 Gm. 160,000 units	Stupor, hematemesis, edema, acidosis, choroiditis, uremia
1:640	15			PABA Penicillin	24 Gm. 160,000 units	
1:160	8			PABA	24 Gm.	
1:320	6	1:64	23	PABA Penicillin	24 Gm. 240 000 units	
1:1,280	16	1:64	20	Oxytetracycline	1 Gm.	Edema, proteinuria, convulsions, carditis
1:160	10			Oxytetracycline	1.5 Gm.	
1:160	5			Oxytetracycline	1.5 Gm.	
1:160	15	1:32	15	Chloromycetin	1.5 Gm.	Edema, peripheral polyneuritis
1:320	8			Chloromycetin Oxytetracycline	1 Gm. 1 Gm.	
neg.	14	1:8	16	Chloromycetin	2 Gm.	
1:320	21	1:64	28	Chloromycetin	1.5 Gm.	
neg.	12			Oxytetracycline Chloromycetin	1.5 Gm. 1.5 Gm.	
1:640	12	1:4	18	Chloromycetin Oxytetracycline	1 Gm. 1 Gm.	Edema, transient high NPN, proteinuria
1:160	11			Chloromycetin	0.5 Gm.	
1:2,560	15			Tetracycline Chloromycetin	0.4 Gm. 0.5 Gm.	
neg.	24			Chloromycetin	3 Gm.	Edema, ECG consistent with myocarditis
1:1,280	10			Tetracycline	1 Gm.	Edema, ECG consistent with myocarditis
1:80	25			Chloromycetin	1 Gm.	Edema, hematemesis

be demonstrated, platelet counts were adequate, and the bleeding time was within normal limits. Tourniquet tests were regularly positive.

One patient showed evidence of impaired vision, and examination of the eye grounds revealed changes consistent with acute choroiditis.

Patient D. S. had convulsions during the acute febrile stage of the disease. There was no history of previous seizures in this case.

Patient J. J. developed signs of right peroneal palsy on the fourteenth day after onset. Hypesthesia was present at the base of the second toe, and there was pain on dorsiflexion of the foot. This gradually regressed over a two-week period. Foot drop was still present ten days later at the time of discharge. No follow-up observations were possible on this patient.

In two other patients, Z. S. and A. W., diminished heart sounds and tachycardia led to electrocardiographic studies which were interpreted as being consistent with myocarditis. A return to normal of the electrocardiogram was observed after clinical recovery in both cases.

EPIDEMIOLOGIC DATA

All but four patients in this series came from rural areas heavily infested with ticks. One patient, Z. S., became sick one week after returning from summer camp. Patients D. S. and G. S. were siblings and were hospitalized within a two-day period. A tick was removed from one of these children's scalp eight days before the onset. A definite history of tick bite was obtained in seven cases. The seasonal incidence is well demonstrated in Table I. The disease occurred during winter months in only two patients, T. B. and C. W. No explanation for the striking predominance of white patients in this series can be advanced, especially since these cases were observed in a charity hospital serving a predominantly Negro population.

TREATMENT

Table I summarizes dosages and types of the various antibiotics used as they became available or were advocated as drugs of choice. In the majority of cases, doses listed were started immediately after admission. In patients D. S. and B. H., initial treatment also included streptomycin and sulfadiazine, employed in order to achieve broad coverage while waiting for the cerebrospinal fluid culture reports.

We first used broad-spectrum antibiotics in 1949, and their introduction appears to have brought about a significant shortening of the febrile period of the disease. However, the number of cases in this series is too small to permit adequate evaluation of the respective merits of the various types of broad-spectrum antibiotics. Tabulation of the results obtained in our series is given in Table II, using the date of defervescence as an index of activity. The temperature curve, however, does not always parallel the clinical course or reflect the severity of the underlying complications.

Early diagnosis and treatment probably have some protective action against complications. Out of twelve noncomplicated cases, five were seen prior to or on the fifth day after onset, while only one case out of eight complicated cases was seen as early as the fifth day after onset. In complicated cases the average time which

TABLE II. AVERAGE NUMBER OF DAYS OF FEVER AFTER INITIATION OF TREATMENT

	DAYS	CASES
Penicillin and sulfadiazine	13	3
Penicillin and PABA	9	2
PABA	4	1
Oxytetracycline	7	3
Tetracycline	6	1
Chloromycetin	6	6
Oxytetracycline and Chloromycetin	7	3
Tetracycline and Chloromycetin	1	1

elapsed before initiation of treatment was eight and one-half days. It was seven days in noncomplicated cases.

The incidence of complications was two in six cases seen before 1949, and six in fourteen cases seen after the introduction of antibiotics. Our only death occurred in a patient who did not receive antibiotics.

We regard tetracycline as the drug of choice due to the paucity of its side effects and absence of depressant action on the bone marrow.[12] It should be stressed that antibiotic treatment must be continued for a period of at least three days after the return of temperature to normal in order to avoid relapses.[8]

Supportive therapy is of paramount importance in the pediatric patient. Its main points are the correction of electrolyte imbalance by fluid administration and the replacement of plasma lost to the tissues. We have not administered cortisone to any of our patients, although its use with concomitant antibiotic therapy has been recommended by others.[13]

SUMMARY AND CONCLUSIONS

1. Eighteen proved and two probable cases of Rocky Mountain spotted fever were observed in children during the past twelve years.

2. Factors permitting easy diagnosis in most cases include: (a) history of tick bite; (b) fairly constant and typical rash; and (c) positive agglutination and complement fixation reactions.

3. Meningococcemia is the major differential diagnostic hurdle but is readily excluded.

4. Broad-spectrum antibiotics have improved the prognosis, but supportive therapy still plays an essential role in children.

5. Choice of antibiotics is discussed.

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SUBSEQUENT MENTAL DEVELOPMENT OF CHILDREN WITH LEAD ENCEPHALOPATHY, AS RELATED TO TYPE OF TREATMENT

J. Edmund Bradley, M.D., and Ruth J. Baumgartner, M.A.
Baltimore, Md.

THE therapeutic use of, first, 2,3-dimercaptopropanol (BAL)[1] and, subsequently, the chelate, calcium disodium ethylenediaminetetra-acetic acid (EDTA)[2] have resulted in the recovery of a significant number of children with lead encephalopathy. A number of investigators have reported on the later development of children who have recovered from lead encephalopathy.[3, 4] In general, follow-up studies have revealed neurologic sequelae, mental retardation, and visual-motor disabilities. These studies have been carried out without regard to type of treatment. However, it has been suggested that patients treated with EDTA have a significant reduction in neurologic sequelae and mental retardation.[2, 5]

The purpose of this study is to compare several areas of intellectual functioning in two groups of children with lead encephalopathy, one treated with BAL and one with EDTA.

METHOD

Eighteen Negro children who had been admitted to the University of Maryland Hospital during the past five years and treated with lead encephalopathy were selected for study. Nine of these were treated with BAL; nine received EDTA. All patients in each group satisfied the criteria of lead encephalopathy, viz., admitting complaint of convulsions, lethargy, or irritability; a history of pica for lead-containing substances; blood lead values in excess of 0.05 mg. per cent (range 0.052 to 0.53 mg. per cent), and radiographic evidence of heavy metal intoxication. Determinations of lead content of the reported ingested substance revealed a toxic amount of lead. Intragroup treatment was consistent: for BAL cases, the dosage was 3 mg. per kilogram for 12 days; for EDTA cases, 1 Gm. per 15 Kg. was adminstered intravenously for a period of five days.

The subjects of both groups were of low socioeconomic status and were equally divided as to sex. The mean age of the BAL-treated group at the time of hospitalization was 29 months; that of the EDTA group, 26 months. Of the BAL group, three were classified as severely ill, the remainder as moderately severe. The EDTA group was generally comparable in that it included 4 severely ill and 5 moderately severe.

The interval between hospitalization and follow-up averaged 3.77 years for the BAL-treated group, with a range of 3 to 5 years. For the EDTA group, the mean interval was 3.0 years, with a range of 2 to 4 years.

From the Department of Pediatrics, University of Maryland, School of Medicine.

Supported by grant-in-aid (B-750) from Department of Health, Education and Welfare.

Psychological tests and complete neurological examinations were administered to all children in both groups. All neurological examinations were essentially negative. Psychological tests given to all subjects were the Stanford-Binet (Form L), Goodenough Man Drawing, and the Bender-Gestalt Visual Motor Test.

In view of what has often been observed and written of the hyperactive, distractible behavior of postencephalitic cases, personality and behavioral information would have been desirable.[6] However, as some of the children were too young for appropriate measures at the time of testing, it was decided to limit this study to cognitive aspects of functioning.

RESULTS

Results of the tests for both groups are presented in Tables I and II. As no appropriate method was available for evaluating Bender results quantitatively, they have been rated clinically as to deviation from normality by one of us (R. B.) experienced in dealing with the design reproductions of brain-damaged children. Three categories were used: normal, borderline (suggestive of brain-damage), and severe visual-motor dysfunction. Only chronological age and Binet mental age were known at the time of evaluation. Such frequently assumed indications of organic damage as distortions of the patterns, rotations, dissociations, and

TABLE I. PSYCHOLOGICAL TEST RESULTS FOR BAL-TREATED GROUP

CASE	SEVERITY OF ILLNESS	AGE WHEN TESTED (YEARS)	BINET I.Q.	GOODENOUGH I.Q.	BENDER RATINGS OF VISUAL-MOTOR IMPAIRMENT
1	Severe	6.0	74	63	Severe
2	Moderately severe	8.0	96	73	Borderline
3	Moderately severe	3.0	106	73	Borderline
4	Moderately severe	8.0	106	101	Borderline
5	Moderately severe	4.0	84	90	Normal
6	Moderately severe	5.7	88	105	Normal
7	Severe	4.8	69	71	Severe
8	Severe	7.5	96	80	Severe
9	Moderately severe	4.7	87	73	Borderline
Mean		5.74	89.55	79.88	
Standard deviation			11.62	14.69	

TABLE II. PSYCHOLOGICAL TEST RESULTS FOR EDTA-TREATED GROUP

CASE	SEVERITY OF ILLNESS	AGE WHEN TESTED (YEARS)	BINET I.Q.	GOODENOUGH I.Q.	BENDER RATINGS OF VISUAL-MOTOR IMPAIRMENT
1	Moderately severe	5.5	89	103	Normal
2	Moderately severe	3.7	102	102	Normal
3	Moderately severe	6.8	80	91	Normal
4	Severe	4.0	105	81	Severe
5	Severe	5.7	109	128	Normal
6	Moderately severe	5.6	94	99	Borderline
7	Severe	4.7	97	71	Severe
8	Severe	5.2	102	128	Borderline
9	Moderately severe	4.7	112	102	Borderline
Mean		5.1	98.88	101.55	
Standard			9.53	17.88	

perseverations were considered.[7] Significance tests of the intelligence test results of BAL- and EDTA-treated groups are presented in Table III.

TABLE III. COMPARISON OF BINET AND GOODENOUGH (INTELLIGENCE QUOTIENTS) OF BAL- AND EDTA-TREATED GROUPS

GROUP	BINET I.Q.		GOODENOUGH I.Q.	
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION
BAL	89.55	11.62	79.88	14.69
EDTA	98.88	9.53	101.55	17.88
Difference	9.33		21.67	
t	1.93		2.66	
P	.05		.02	

While the Binet scores of the EDTA group are superior to those of the BAL group, the difference might be explained on a chance basis. The mean scores of both groups are within the range that could be expected from a low socioeconomic Negro population. Examination of Binet scatter patterns revealed no definite trends. Although some subjects showed memory difficulties, this was not characteristic of either group as a whole.

The obtained Goodenough (Intelligence Quotient) difference between the BAL and EDTA groups is significant at a 0.02 level of confidence, i.e., it would be expected to occur on a chance basis only 2 times out of 100. In a comparison of Goodenough (Intelligence Quotients) for the two groups, more similar differences to those obtained on the Binet might be anticipated, as the two measures are generally highly correlated in a normal population of this age range. The Goodenough, however, is usually considered to be heavily weighted with visual-motor ability so that the obtained difference may reflect greater disability of the BAL group.

Reference to the individual Bender ratings presented in Tables I and II again indicates somewhat less impairment of the visual-motor function in the EDTA group. Of the 9 EDTA cases, 4 were considered normal, 3 borderline, and 2 severe. Only 2 of the 9 BAL-treated cases were rated normal, 4 borderline, and 3 severe. As both the Bender and the Goodenough sample visual-motor ability, considerable agreement might be expected, and this was found to be the case. A rank order correlation of + 0.57 was obtained. (Bender tests were ranked according to clinical estimate of degree of severity.)

DISCUSSION

General intelligence tests revealed no significant residual deficit in over-all ability for the lead poisoning groups as a whole. This finding is not in accord with the suggestion of Millican and associates[8] that original brain damage and retardation may be contributory to pica and subsequent lead encephalopathy. In only two cases of the BAL group was general intelligence significantly below normal at the time of follow-up.

The finding that visual-motor deficit is the only prominent residual in all the lead poisoning cases is in agreement with the conclusion of Thurston and associates.[3] In the BAL-treated group as a whole, visual-motor difficulties are more frequent than in the

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EDTA group. However, it should be noted that several of the EDTA group evidence gross visual-motor impairment. While it would seem that EDTA is contributory to offsetting these undesirable sequelae, it obviously cannot reverse the course of brain damage.

It should be recognized that factors other than the EDTA treatment per se may have influenced these findings. The EDTA cases were generally hospitalized in more recent years; although half were concurrent, better methods of management may be reflected to some extent.

The severity of the encephalopathy must be considered also. Inspection of the individual cases presented in Tables I and II reveals that the 3 BAL cases rated severely ill show considerable visual-motor impairment on the Bender. Among the EDTA group, the correspondence is less striking, but the Bender reproductions of 2 of 4 cases classified as severe show marked visual-motor difficulty. Goodenough Intelligence Quotients were also examined for possible relationship with severity of illness. For the BAL group, a bi-serial coefficient of correlation of + 0.65 was obtained between these variables (SE equals 0.29). However, the significance of this bi-serial r is greater than the 0.05 level and it can be considered only suggestive of a relationship. Similar correlation computations between severity of illness and Goodenough I.Q. for the EDTA group point to no relationship (r bis equals – 0.09).

Several other factors were examined for their possible relationship to severity of psychological residual. No correlation was found between duration of pica or duration of symptoms before treatment with subsequent deficit. These data were based on historical information, however, which is recognizedly unreliable. Again, no relationship was apparent between age at illness and later development. Blood lead levels determined at time of hospitalization and throughout observation also appeared to be noncontributory.

SUMMARY

Nine BAL-treated cases of lead encephalopathy were compared with nine EDTA-treated cases 2 to 5 years after hospitalization. Psychological tests were administered to all in an effort to determine possible differences in residual deficit as related to type of treatment.

1. No significant differences were found between mean ratings of both groups in general intelligence. Both averaged within the normal range.

2. The EDTA group was superior to the BAL group on visual motor tests at significantly better than chance expectancy.

3. Among BAL-treated cases, the severity of visual-motor impairment generally corresponding to severity of illness. Visual motor dysfunction was found less frequently among the severe EDTA cases.

While it is suggested from this study that EDTA may be more effective in reducing undesirable psychological residuals, the possibility of their occurrence remains despite type of treatment.

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In the Days of "Green Sickness"

It is an undoubted fact that in many, very many cases, the function of lactation is imperfectly performed. This deficiency arises from two sources, imperfect development of the genital organs (including the mammary glands), and general debility of the vital functions. The season of puberty extending from 13 or 14 to 18 or 20 years of age, is the only period during which the generative apparatus can be well developed. If this season be lost, the evil can never be repaired. The development must occur *then* or *never*. How important, then, that girls should enter upon and pass through this season under the most favourable physical conditions. Good food, good air, sunshine, muscular exertion, everything that tends to bodily vigour, should be secured to them during this period of life. Sedentary occupations, excessive mental exertion, late hours, insufficient sleep, are evidently most unfavourable to development. And yet in this last sentence we have sketched the history of a very large number of girls of all classes.

CUMMING, WM. HENRY: ON NATURAL AND ARTIFICIAL LACTATION, AM. JOURNAL OF MEDICAL SCIENCES, VOL. 36, 1858.

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FAMILIAL TREMBLING OF THE CHIN

WILLIAM B. WADLINGTON, M.D.
NASHVILLE, TENN.

FAMILIAL trembling of the chin has been described in four families in the literature. Grossman[1] was the first to report this entity in the American literature. He traced the genealogy of his cases for four generations. Seven members exhibited quivering chins and no other detectable neurological abnormalities. Three members of the family also had otosclerosis. Various published pedigrees of families with otosclerosis[2, 3] show that this gene is passed as a simple dominant, as is the gene which causes trembling chins.

It is the purpose of this paper to describe the history, electroencephalographic findings, and treatment on another family with trembling of the chin.

CASE REPORTS

Mrs. A (shown as II 4 in Fig. 1) is 40 years old and the mother of four boys (IV 1, 2, 3, 4). She has always enjoyed good health. For as long as she can remember, she has had trembling of the chin which she described as like a "rabbit's nose." She recalls that this was a source of embarrassment to her in earlier life as it was often misinterpreted as the onset of a tearful episode. "Sometimes," she stated, "I may go for days and my chin will be still and then when I become anxious or excited my chin will begin to tremble."

The physical and neurological examinations are normal. The description of her electroencephalogram is as follows: "This record was regular with a dominant frequency ranging from about 9 to 14 per second. Amplitudes rarely exceeded 60 mμ volts. There were no significant asymmetries or abnormal wave forms among the 14 leads employed. Some irregular sinusoidal slowing developed on overventilation with waves ranging as slow as 2½ per second. Some exceeded 150 mμ volts. All leads were involved. The record returned to its pre-overventilation level slowly over a period of about two minutes. There was a similar reaction association with the second period of overventilation after sugar by mouth. Again the record cleared during the second minute after overventilation ceased."

Interpretation: "This record is a border-line normal tracing on the basis of its reaction to overventilation with relatively short clearance time. No definite focal abnormalities were made out." Mrs. A's chin trembled intermittently during the electroencephalogram but there were no accompanying or associated abnormal waves noted at these times. She had some drawing of her hands and inability to speak for about 5 seconds after overventilation.

Mrs. A's first child (IV 1) is 11 years old. He had always been in good health and has never had trembling of the chin or any other difficulties. His electroencephalogram* (Fig. 2) was described as follows:

From the Department of Pediatrics, Vanderbilt University School of Medicine, Seizure Clinic.

*All EEG readings were done by Dr. James Ward, EEG Laboratory, Vanderbilt University School of Medicine.

"This record was mildly irregular with amplitudes that varied from 30 to more than 125 mμ volts. The highest waves were in the occipital leads. The dominant frequency ranged from about 7 to 14 per second. No significant asymmetries or definite abnormal wave forms were seen among the 14 head leads employed. The record increased in amplitude and in irregularity on overventilation and slowing occurred in long trains. Some of the

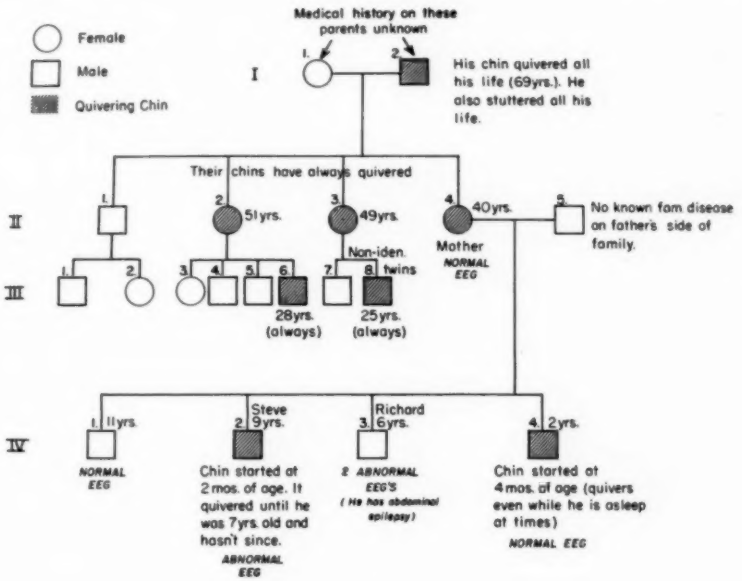

Fig. 1.

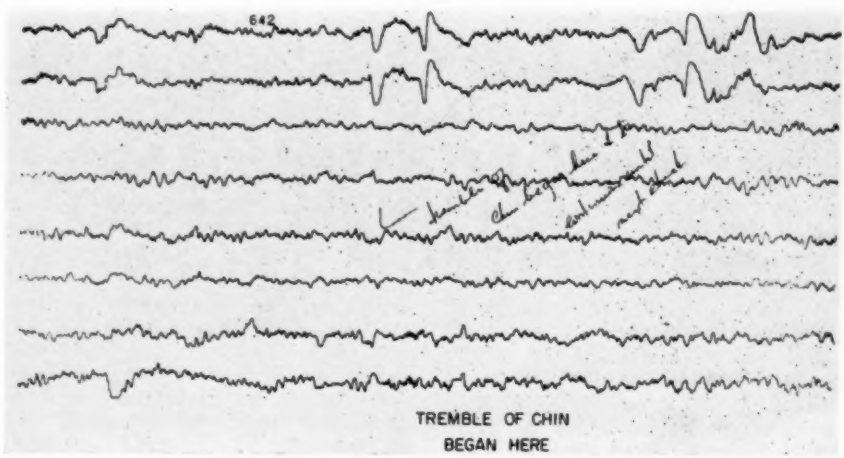

Fig. 2.

waves were as slow as 2½ per second and they exceeded 200 mμ volts. The record returned to its pre-overventilation level within about 1 minute after overventilation ceased. There was a similar reaction associated with a second period of overventilation after sugar by mouth. It required about 2 minutes for the record to return to its pre-overventilation level. Considerable irregularity was recorded in the remaining portion of the tracing."

Interpretation: "This record is probably within normal limits. There were no focal abnormalities. While the reaction on overventilation ceased and therefore may not be an indication of a significant generalized cortical dysfunction."

seen among the 14 head leads employed. Several bursts of waves in the order of 4 per second were recorded. These, too, were not in excess of 100 mμ volts. Marked slowing developed on overventilation. This had an episodal quality. The waves were as slow as 2 to 3 per second and exceeded 200 mμ volts in amplitude. All leads were involved. It required several minutes for the record to return to its pre-overventilation level and a similar reaction occurred during a second period of overventilation after sugar by mouth."

Interpretation: "This record is outside of normal limits, I believe, on the basis of the slowing prior to overventilation as well as the marked re-

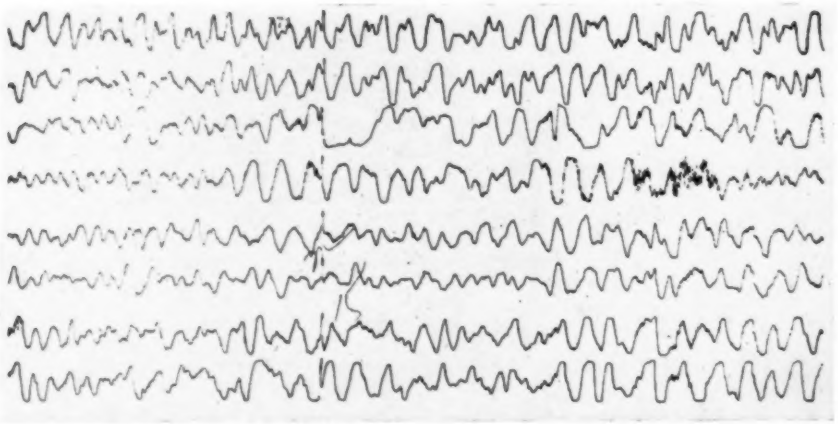

Fig. 3.

Her second child (IV 2) is 9 years old. His chin started quivering when he was 8 weeks old and continued intermittently for the next seven years, when it spontaneously stopped. There has been no recurrence for two years.

Description and interpretation of his electroencephalogram (Fig. 3) are as follows: "This record was mildly irregular with frequencies that ranged from about 6 to 15 per second. Amplitudes rarely exceeded 75 mμ volts. No clean out localized abnormal wave forms or significant asymmetries were

action associated with overventilation and its long clearance time. There were no clean out focal abnormalities seen."

Mrs. A's third child (IV 3) is 7 years old and has never had a trembling chin. He had a complete workup in Vanderbilt Hospital on Nov. 1, 1956, because of recurring abdominal pain. His complete history, physical examinations, and laboratory workup have been previously reported,[4] as representative of abdominal epilepsy. His bouts of abdominal pain have

been controlled satisfactorily by phenobarbital and dilantin. His second electroencephalogram (Fig. 4), taken two weeks after all medications were stopped, was interpreted as follows: "This record was quite irregular with waves ranging from 4 to 7 per second occurring in trains. Faster frequencies as high as 15 per second were recorded. Amplitudes were rarely in excess of 100 mμ volts. No definite asymmetries were seen among the 14 leads employed. A marked reaction occurred with overventilation. It consisted of slowing in the order of 3 to 5 per second with amplitudes exceeding 200 mμ volts. All leads were involved. The record to its pre-overventilation slowly after overventilation ceased. There was a tendency for higher amplitude to occur on the right in the posterior quadrant than elsewhere. A similar reaction was associated with a second period of overventilation after sugar by mouth."

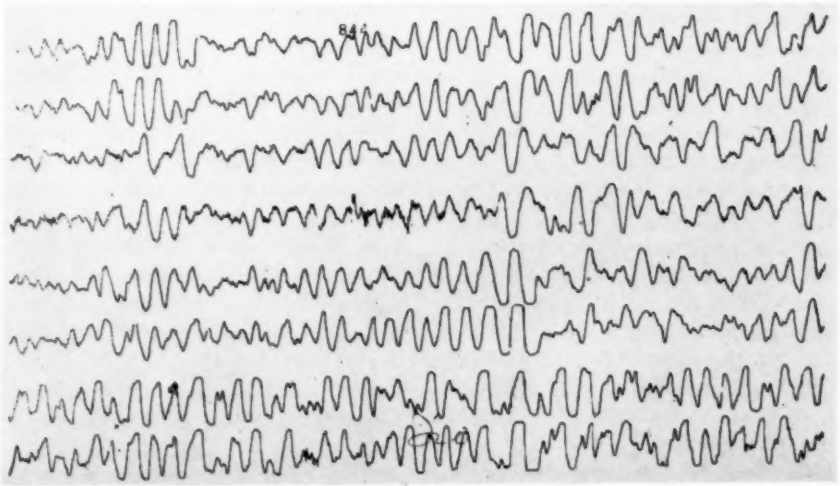

Fig. 4.

Interpretation: "This record is outside of normal limits and points to an episodical type of generalized cortical dysfunction. The record is somewhat improved over the previous one."

The fourth and youngest child (IV 4) is 2 years old. Trembling chin was first noticed at 4 months of age and occurs while he is asleep. However, excitement is usually the trigger mechanism that starts these involuntary chin movements. His electroencephalogram showed the following: "This record was mildly irregular with frequencies ranging from about 5 to more than 12 per second. Amplitudes rarely exceeded 100 mμ volts. The slower waves were present in all leads in a diffuse fashion. At times, however, they tended to be somewhat higher on the right. This difference was not a great one."

Interpretation: "The changes in this record are exceedingly mild and it is difficult to tell whether they represent an abnormality or not. There may be a mild generalized non-episodal slowing with possibly some amount on the right side."

Mrs. A's two older sisters (II 2, 3) have always had trembling chins. The exact age of onset of this condition is unknown to them. One sister (II 3) had fraternal twin boys with only one of the boys (III 8) manifesting this

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finding. Mrs. A's father's (I 2) chin quivered all his life. He died at the age of 69 years and during this time he was constantly bothered with a moderately severe case of stuttering. The medical history is not known about his or his wife's (I 1) parents. There is no known history in the family tree of epilepsy, mental retardation, migraine, or other neurological abnormalities.

DISCUSSION

In 1930 Frey[5] described five generations of a family with the abnormality of quivering chins. Their pedigree reveals there were 55 affected, 45 normal. Some of the children described by Frey had trembling of their chins noted in the first day of life. In others it did not start until 1 or 2 weeks of age and in others much later in life. An occasional member of the family reported would have an apparently spontaneous remission of his "disease" (as did the child [IV 2] reported in this communication). Still another female member of this family had experienced no abnormal movements of her chin for one year following termination of her first pregnancy when uncontrollable movements of her chin recurred especially during periods of anger or deep concentration. The only other abnormality in this family tree was one case of nystagmus and several instances of intolerance for alcoholic beverages even in moderation.

The trembling of the chin may last for a few seconds or for several minutes. The tremor may be either fine or coarse movements and not particularly related to the precipitating cause. The trembling of the chin is perpendicular and at the rate of two or three times per second. In most cases some emotional stimulus such as anxiety, anger, or depression acts as the trigger mechanism. It has been noted that the only stimuli which will act as a precipitating cause in some individuals are periods of concentration, awakening abruptly, or playing a violin.

The pedigree of the family herein described is shown in Fig. 1. It appears that the trait is transmitted in a simple dominant pattern as has been reported by Ganner[6, 7] and Westphal.[8] Our pedigree, however, does not rule out the possibility that this trait might be due to a sex-linked dominant gene.

Treatment for this condition has been unsatisfactory in the past. Frey used faradic current and ultraviolet light to no avail. Psychotherapy has been thought to be helpful at times. Since two of the children (IV 2, 4) had abnormal electroencephalograms, a therapeutic trial was made with anticonvulsant therapy.

Mrs. A (II 4) was started on dilantin, 0.1 Gm. twice a day. Her children (IV 2, 4) were also started on dilantin (10 mg. per kilogram per day). They were kept on this treatment program for the next few months with favorable results. There appears to have been a decrease in the frequency and duration of the chin trembling; however, the period of follow-up has been too short to draw any definite conclusions.

Since anxiety and emotional upsets have acted as trigger mechanism for many of these attacks in the past, it was decided to discontinue the dilantin so that the effects of a tranquilizer could be evaluated. Accordingly, the above patients were started on hydroxyzine hydrochloride (Atarax*).

*J. B. Roerig & Co.

The 2-year-old boy received 10 mg. of Atarax twice a day. His 9-year-old brother received 20 mg. twice a day and their mother was given 30 mg. twice daily. No side effects were noted on this dosage and this therapy was continued for two months.

Again Mrs. A noted that she and her children had a decrease in the frequency and duration of their bouts of quivering chins. She felt she was much improved by the medication because she said, "I do not get as excited or anxious as I did and that is what brought on most of my attacks."

A record of the exact number of the attacks before and after treatment would be very desirable, but the family failed to keep a record. Follow-up electroencephalograms were planned while on therapy, but the family moved to another city and were not available for further follow-up. It was not felt that either type of therapy was continued long enough (or with various dosages) to evaluate which treatment schedule was superior.

SUMMARY

1. This is the second family to be reported in the American literature with familial trembling of the chin.

2. This is the first report of electroencephalograms of these patients.

3. Further therapeutic trials with tranquilizers or anticonvulsant therapy should be evaluated.

I express my thanks to Dr. James Ward, Dr. Amos Christie, and Dr. Harris Riley for their help and suggestions in the preparation of this paper.

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COMA IN A CHILD FOLLOWING USE OF ISOPROPYL ALCOHOL IN SPONGING

EDWARD H. SENZ, M.D.,* AND DONALD L. GOLDFARB, M.D.,**
SAN FRANCISCO, CALIF.

THE differential diagnosis of coma in a child should include alcohol intoxication due to alcohol sponging. Garrison[1] reported the development of coma in a 22-month-old boy who had been sponged to reduce fever with about 1¼ pints of isopropyl alcohol in a small, unventilated cubicle. This boy's blood alcohol level was 128 mg. per 100 ml. of blood. He regained consciousness slowly but was said to have recovered completely at the end of 24 hours.

This is a report concerning a similar occurrence.

CASE REPORT

S. C., a 2½-year-old white girl, became ill with fever on Dec. 6, 1957. A physician diagnosed an ear infection and prescribed aspirin, tetracycline syrup, and alcohol sponging. At 7:00 P.M. on December 6, she was given 2½ grains of aspirin. At 12:00 midnight a towel was saturated with 12 ounces of 70 per cent isopropyl alcohol and wrapped about the patient. A second, dry, towel was placed over the first, and the patient was placed in bed with her aunt. A window in the bedroom was partly open. At 8:00 A.M. on December 7, the patient could not be aroused. She arrived at San Francisco Hospital at 9:25 A.M., limp and totally unresponsive.

She weighed 25 pounds. Her temperature was 97° F., pulse 160 and regular, and respirations 30 and extremely shallow. Blood pressure was 100/60. There was a sweetish smell, resembling acetone, on her breath. Her pupils were small and did not respond to light. The corneal reflexes were present but no other reflexes, superficial or deep, could be obtained. The neck was supple. An x-ray picture of the chest showed no disease. Routine blood counts were normal. Urinalysis was negative except for 1 plus acetone. A ferric chloride test for salicylates in the urine was negative. Cerebrospinal fluid was normal, but was under a pressure of 270 mm. of water. Because of poor pulmonary ventilation an endotracheal tube was inserted. At 10:30 A.M. the patient was apneic for a period of five minutes and was given artificial respiration. At 11:00 A.M. blood was drawn for blood alcohol determination. At 12:00 noon the patient vomited coffee-grounds material. At 12:30 P.M. spontaneous movements were noted for the first time. At 1:30 P.M. the endotracheal tube was removed. At 10:00 P.M. she cried and called for "Mama." Her treatment was purely supportive, with intravenous fluids, oxygen, and antibiotics. By the following morning she was fully conscious. She remained irritable and inactive for several more days.

From the Department of Pediatrics, Stanford University School of Medicine, San Francisco, and the San Francisco Hospital, Department of Public Health.

*Assistant Professor of Pediatrics, Stanford University School of Medicine; and Chief, Stanford Pediatric Service, San Francisco Hospital.

**Assistant Resident in Pediatrics, Stanford University School of Medicine.

The blood contained 130 mg. of isopropyl alcohol per 100 ml.

DISCUSSION

We believe that this child's coma was the result of inhalation of isopropyl alcohol.

Investigations of the pharmacologic action and toxicity of isopropyl alcohol have been summarized in detail by von Oettingen.[2] Its most important toxic effect is central nervous system depression. Isopropyl alcohol is twice as toxic as ethyl alcohol and produces greater and longer-lasting narcosis than does ethyl alcohol. It is absorbed readily through the lungs but probably not through the skin (at least in experimental animals). It is oxidized to acetone, perhaps quantitatively, and it is interesting to speculate that the depression of the central nervous system may be due to the acetone as well as to the alcohol itself.

CONCLUSION

The physician who orders alcohol sponging for the reduction of body temperature should be aware that serious poisoning can occur as a result of inhalation of alcohol fumes. Further, the history of a comatose child should include specific inquiry regarding alcohol sponging preceding the coma.

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PERFORATED DUODENAL ULCER IN AN INFANT

CHRIS T. OECONOMOPOULOS, M.D.
BOSTON, MASS.

DUODENAL ulcers in infants are rare; however, it appears that some may have been overlooked in the past. Since Cruveilhier's[1] first description of peptic ulcers in infancy in 1829, increasing numbers of cases have been reported in the literature.

In 1941, Bird, Limper, and Mayer[2] reviewed all reported cases of peptic ulcers in infancy and childhood. Of the 243 cases found in the world literature, 43 cases had occurred in the age group from 15 days to 1 year. The ratio of duodenal-pyloric ulcers to gastric ulcers in this series is approximately one to one.[2] It is of interest that this ratio differs so markedly from that of adults, which is usually expressed as one gastric to nine duodenal ulcers. The sex distribution appears to be almost equal.[7] In an autopsy review of 8,260 patients dying because of peptic ulcer disease at Mayo Clinic,[3] only two children were found with peptic ulcer.

Three types of ulcers are generally recognized in infancy and childhood.[4] The first type is found within the first two weeks after birth. It is an acute ulcer associated with melena neonatorum[5] and is frequently seen in newborn normal-term infants.[6] The second type occurs between the ages of 2 weeks and 1 year and is acute or subacute. The third type occurs in children between the ages of 1 and 9 years and is chronic in type. The latter type usually fails to cause symptoms characteristic of peptic ulcer in the adult until the child reaches the age of 10 or 12 years.

The recognition of the ulcer during life is a problem that presents great difficulty. Approximately 30 per cent of duodenal ulcers in infancy and childhood perforated, according to a review of Hutchins.[8]

In view of the comparative rarity of this condition, the following case of duodenal ulcer with perforation in an infant is presented. The case is the first that came to autopsy in the Mallory Institute of Pathology, Boston City Hospital, between the years 1933 and 1958, and is included in a series of 1,672 post-mortem examinations on children under the age of 13 years.

CASE REPORT

M. C., a 7-week-old white male infant, was brought to the Boston City Hospital severely dehydrated, in shock, and in a moribund state. Four hours prior to admission, the mother noticed that the infant appeared "to gag," then threw up approximately a tablespoonful of milk curd. Shortly thereafter, he passed 150 to 200 c.c. of a yellow, watery diarrhea and, according to the mother, "He didn't look right."

The history revealed that the infant was a normal full-term child, weighing 2,955 grams. There was no asphyxia and the infant cried immediately. Physical examination was not remarkable save for a primary hypospadias. The mother, aged 32, had previously given birth to four full-term infants. Her blood Wassermann was negative. During the first few days the infant had ill-defined "feeding problems"; however, he was discharged on the sixth day of life and thereafter ate

From the Mallory Institute of Pathology, Boston City Hospital.

regular feedings without vomiting or any suggestion of abdominal pain. Stools were regular, with usual color, and there were no episodes suggestive of gastrointestinal bleeding. At 3 weeks of age he weighed only 3,260 grams and appeared "thin."

Physical examination on admission revealed a pale, severely dehydrated baby with a blood pressure of 40/0, pulse 100, respirations 40, and temperature 97° F. The lungs were clear to auscultation and percussion. Heart was normal. The abdomen was moderately distended, although soft to palpation, with normal bowel sounds. The rectal ampulla contained soft yellow stool. Genitalia showed primary hypospadias. Neurological examination was negative.

Fig. 1.—Roentgenogram taken after the ingestion of barium. It reveals collection of barium at the prepyloric region. The slightly deformed shape of duodenal cap raised the possibility of ulcer, although no definite crater is seen.

Laboratory data revealed a white blood cell count of 18,900, with 47 per cent neutrophils. White count rose progressively to 20,220 over the next two days. Hemoglobin was 14.8 grams per 100 ml. and hematocrit 37 per cent. Platelets were adequate. Stools tested six hours after admission gave a 4 plus guaiac reaction and remained 4 plus for the following three days. Serum electrolytes were normal. The nonprotein nitrogen was 51 mg. and dropped to 23 mg. the third day. Serologic test for syphilis was negative. Stool culture on admission showed no growth; when repeated the third day, culture grew out *Escherichia coli*. Urine was negative. A 24-hour urine contained sodium 17 mEq. per liter and chlorides 27 mEq. per liter.

Clinical Course.—The night of admission he passed several bloody stools and vomited approximately 40 c.c. of coffee-grounds material. On admission, intravenous fluid was started, then, after the onset of gastrointestinal bleeding, therapy included plasma, whole blood, and vitamin K. Despite continued supportive care, the infant remained critically ill. By the third day distention had decreased and he was started on skim milk and supplementary electrolytes. The bowel sounds, however, were hypoactive and he aspirated once on the fourth day. He had no diarrhea. Chest x-rays were not remarkable. Recumbent and erect films of the abdomen, on admission, were negative, and no free air or obstructive pattern was demonstrated at any time during his hospital course. Barium enema was negative. Upper gastrointestinal series done on the fifth day failed to reveal any pathology, except for a suspicious deformity in the duodenal cap suggestive of ulcer. This deformity was seen in only one spot film (Fig. 1) and no definite crater was visible. There was

no improvement in the patient's condition and he expired quietly on the sixth hospital day.

Autopsy was performed twelve hours after death. The baby was pale and emaciated, weighing 2,760 grams. The abdominal cavity was distended and contained free gas together with 230 c.c. of orange, turbid fluid, with particles of thick material, some of which were adherent to the viscera. Culture of this exudate grew out *B. pyocyaneus*. On the serosal surface of the first part of the duodenum, near the pylorus, a fibrinoid exudate covered an underlying perforation which measured 5 by 6 mm. in diameter (Figs. 2 and 3). Its long axis was longitudinally placed in the posterosuperior wall. The microscopic slides of the ulcer showed an acute perforated ulcer, similar to the adult type. The base of the ulcer shows digestion and necrosis with a layer of fibrin and neutrophils below this (Figs. 4 and 5). The stomach was normal in size and not hypertrophied. The pylorus was unremarkable. There were no post-mortem changes in the duodenum. The rest of the intestine contained a quantity of light food and showed a uniform congestion. The parietal and visceral

Fig. 2.

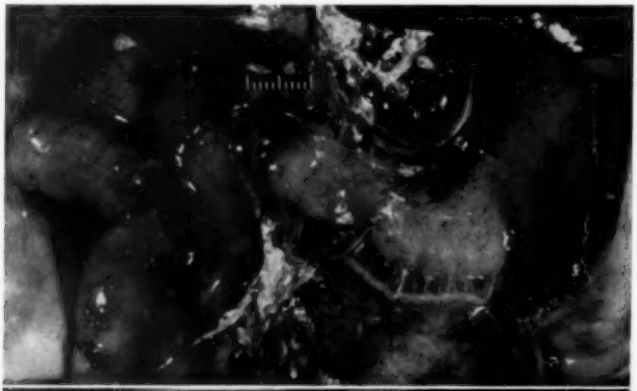

Fig. 3.

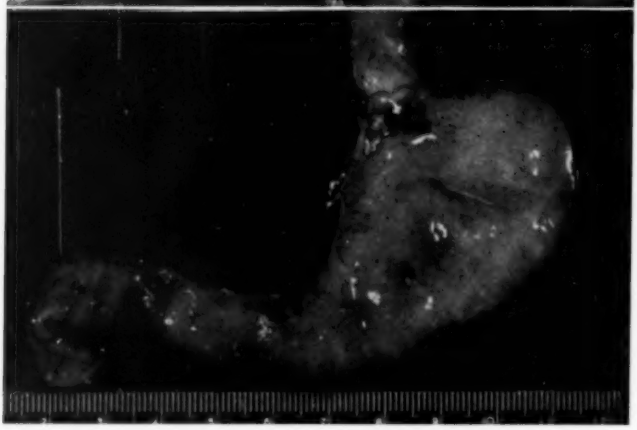

Fig. 2.—The perforated ulcer is clearly seen, with plastic peritonitis in the surrounding tissues.

Fig. 3.—The ulcer is seen immediately distal to the pyloric ring.

peritoneum was markedly hyperemie, and the mesenterie lymph nodes were moderately enlarged. The spleen, liver, panereas, kidneys, and adrenals were normal. The lungs, mieroscopieally, revealed an acute bronchopneumonia

Fig. 4.

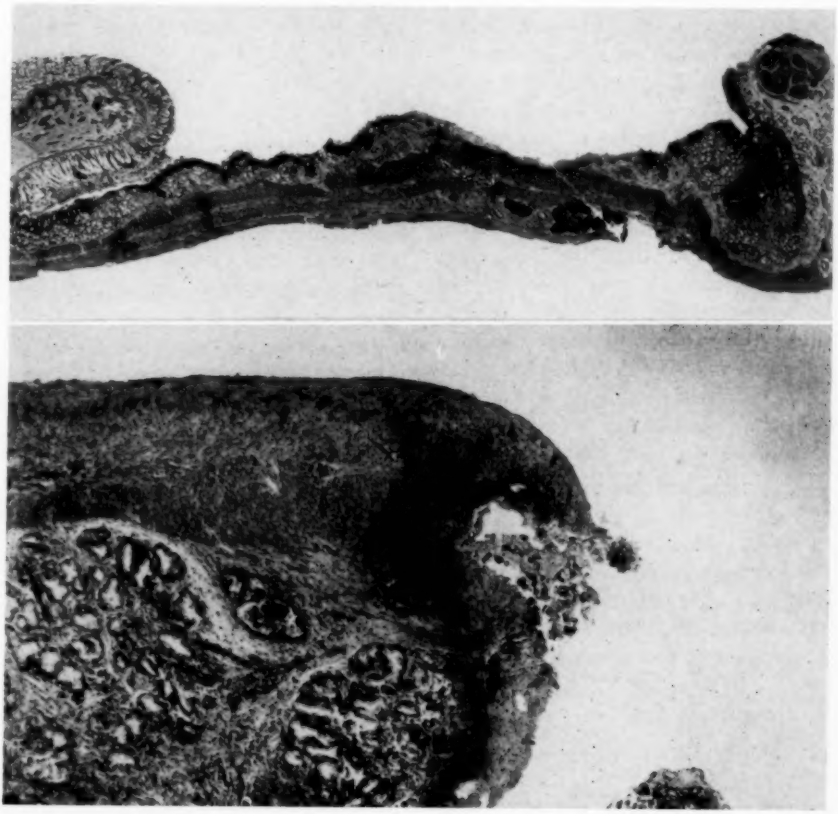

Fig. 5.

Fig. 4.—Photomicrograph showing the base of the ulcer with a thin layer of inflammatory tissue in the mucosa.

Fig. 5.—Photomicrograph at the edge of the ulcer. The ulcer is penetrating down with inflammatory infiltration. (×100; reduced ⅙.)

of the right middle and right lower lobes. The heart presented no abnormalities. The brain was examined by the Neuropathology Department, and sections, especially of the hypothalamic area, revealed no lesions. Two tiny accessory spleens and hypospadias primary were present.

DISCUSSION

Etiology and Pathogenesis.—Multiple etiologic factors are generally considered in the pathogenesis of peptic ulcers in infants. The young infant, as Robbins[9] states, has a predisposition to a variety of disorders different from those encountered in adult life. Environmental and emotional factors apparently operate to a lesser extent in the infant than in the adult. Theile[7] and others consider that ulcers

arise almost invariably after birth. Guthrie[10] gives an excellent review of the literature and suggests vascular occlusion or spasm as a result of birth trauma as being a likely cause of ulcer in the newborn infant. At times it occurs without obvious cause. In infants past the neonatal period, marasmus is the condition most frequently associated with peptic ulcer,[2, 7] although it is more likely that the ulcer is the causative factor of the malnutrition.[11]

The gastric acidity during early infancy deserves special consideration. Miller[12] showed that the maximum acidity is usually reached within twenty-four hours after birth. Thereafter it falls during the first ten days and gradually rises, but does not reach adult proportions until after six months or more of age.

Diverse types of infection may lead to ulceration.[4] Other suspected causes are prolonged or difficult labors, asphyxia, duodenal congestion, and mucosal hemorrhage. It may accompany extensive cutaneous infection or skin burns, nephritis, otitis media, tuberculosis, syphilis, and intracranial lesions.[7, 11] No significant cerebral lesions were observed in the primary ulcers.

Pathology.—Duodenal ulcer in infants is usually a solitary acute necrotizing lesion, located invariably on the posterior wall and proximal to the ampulla of Vater. The lesion may be limited to the mucosa or may extend through the entire thickness of the bowel wall leading to perforation. It has been stated that the necrotizing process is not accompanied by a local inflammatory response[2, 4, 11]; however, in this case the histological picture was that commonly seen in acute peptic ulcers of older children or adults. There is little or no tendency for the destructive lesion to heal. Hemorrhage and perforation are the commonest complications. Hematemesis is more frequent than melena.[13] Peritonitis is fairly common[14] and is generally afebrile, since the duodenal contents are normally sterile and inflammation of the peritoneum is due to mechanical irritation rather than infection.[10]

Clinical Picture and Diagnosis.—The clinical diagnosis of duodenal ulcer in infants is rarely, if ever, made before the occurrence of gastrointestinal hemorrhage, and only a small percentage of ulcers which perforate are diagnosed before death. In the latter instance, sudden abdominal distention is a definite warning sign.[15] Bleeding may be slight or massive and may appear in the form of bright red blood, coffee-grounds vomitus, or as a tarry evacuation. The most important conditions to be differentiated are those of bleeding from the nose or mouth of the infant, bleeding from the nipple of the mother, or other causes of melena,[16] such as esophageal ulcerations, intussusception, Meckel's diverticulum, colitis, rectal polyps, hemorrhagic diathesis secondary to blood dyscrasias. Diagnostic measures of great value in the adult have been shown to be of little value in infants. Roentgenologic examination by means of upper gastrointestinal series during infancy has usually led to failure. Guthrie[10] stated that the barium frequently passes the duodenal cap so rapidly that the crater of the duodenal ulcer cannot be demonstrated. In this case the erect films failed to show pneumoperitoneum. Pendergrass[17] recommends the erect posture to demonstrate this sign. Gastric analysis in

infants is an unreliable diagnostic test.[5] Thus, there is no special sign or symptom or laboratory test including roentgenologic studies that is diagnostic of duodenal ulcer in infancy. Awareness of the existence of this pathological entity, together with signs of gastrointestinal bleeding, may lead to an earlier diagnosis.

Treatment and Prognosis.—Because of the acute and fulminating features, very few of these infants are diagnosed prior to autopsy or are operated upon.[2, 20] Perforation, if diagnosed, demands immediate operation, and the treatment of choice is simple closure.[21] In septic conditions, such as burns, the picture is complicated and no rule can be made for operation. Prognosis is usually poor. Perforation may occur, with death from shock or subsequent peritonitis.

SUMMARY

1. A case of perforated duodenal ulcer in an infant is described.

2. In infants the majority of ulcers either bleed or perforate and may not be diagnosed prior to autopsy.

3. The diagnosis presents great difficulty during life.

4. Duodenal ulcer in infancy is a more important pediatric problem than is generally believed, and awareness of the possibility will lead to earlier diagnosis.

5. A brief review of the disease in the literature is given.

I wish to thank Dr. G. Kenneth Mallory, Dr. Stanley L. Robbins, Dr. Leonard S. Gottlieb, Dr. Anthony E. Boschetti, and Dr. Richard Lennihan for their kind suggestions and criticisms, and Mr. Leo Goodman for the photography.

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UNILATERAL MULTICYSTIC KIDNEY DISEASE

ALTON J. COPPRIDGE, M.D., AND RIGDON K. RATLIFF, M.D.
ANN ARBOR, MICH.

UNILATERAL multicystic kidney disease is recognized almost exclusively in infants and children and is a relatively uncommon condition. The term was first designated by Schwartz,[1] in 1936, in describing a specimen removed from a 7-month-old infant who had been diagnosed preoperatively as having a congenital hydronephrosis or a Wilms's tumor. The chief feature of this lesion, as noted by Schwartz and subsequent authors, is the complete replacement of the kidney by multiple cysts of varying size held together loosely by connective tissue. The appearance is similar to that of a bunch of grapes with complete loss of normal kidney architecture. Usually no grossly identifiable renal tissue is present. The ureter in some instances has been found to be apparently normal (as in the cases presented) but in the majority of reports is absent or atretic. Injection of the ureter or presumed pelvis in a few removed specimens has shown communications with some of the cysts, but in many of the cases reported no intercommunication between cysts could be demonstrated.

Although this condition occurs almost exclusively in infants and children there has been only one reference[2] known to us in the pediatric literature since 1949.[3] We are therefore presenting 2 cases and briefly reviewing the subject.

From the Department of Urology, St. Joseph Mercy Hospital, Ann Arbor, Mich.

ETIOLOGY

There are many different theories advanced as to the etiology of renal cyst formation and polycystic kidney disease as is evidenced by the great diversity of opinion that exists in the literature. Three of the most popular and currently accepted theories are those of Hildebrand[4] (1894), Kampmeier[5] (1923), and Hepler[6] (1930). Hildebrand's theory is that there is malfusion between the secretory and collecting portions of the nephron resulting in cystic dilatation of the proximal portion due to continued secretion of this segment. The thesis of Kampmeier postulates that there is persistence of vestigial cysts which fail to atrophy in normal fashion. The other theory, that of Hepler, postulates that there is localized tubular obstruction with concomitant vascular impairment which results in the formation of cysts. Although several authorities have considered hydronephrosis as a possible basis for the formation of unilateral multicystic kidney disease, no one fully accepted this theory until recently. Fink, Garlick, and Stein,[7] in 1957, postulated that the cysts arose as the result of congenital ureteral hydrocalycosis, probably developing in the 10 mm. stage embryo. Spence,[8] on the other hand, in his excellent

article of 1955 had previously stated that the condition in no way could be considered a hydronephrotic phenomenon.

It is evident from the above that the etiology of this condition remains uncertain and that the defective mechanism in development is not definitely known. However, on the basis of a limited number of cysts and absence of a true pelvis (as in Case 1) one may theorize that the origin of the defect was at the embryo age of about 15 mm. The reason for arrest at this stage is unknown but may have been due to the absence of metanephric stimuli, there being little metanephric tissue present. Histologic study confirms the latter contention and reveals in most instances only atrophic tubules and glomeruli surrounded by fibrous or collagenous tissue. Through lack of containment, which normally comes from maturation of the whole metanephros, and possibly through an abortive effort to function, the calyceal buds distend and their cystic character becomes manifest. The hypothesis that the cysts are due to a hydronephrotic phenomenon has not been substantiated by anatomical evidence (except in one case), and we tend to agree with those authors who feel that this is not a hydronephrotic condition but rather an intrinsic maldevelopment of the kidney itself. The theory of malfusion between the primitive ureteral ramifications and the nephrogenic blastema seems to us to be the most tenable in explaining the etiology of this condition.

CASE REPORTS

CASE 1.—G. S. S., No. 186727, was a full-term male infant who was delivered spontaneously on Oct. 23, 1956, after an uncomplicated labor. A mass in the right flank was discovered shortly after birth on routine physical examination. This was described as being "smooth, firm and 4 × 4 × 3 cm. in size," and it was the impression of the examiner that this represented a right renal mass. The remainder of the physical examination was completely negative except for small bilateral hydroceles. A subcutaneous pyelogram on Oct. 27, 1956, showed a slight cystogram at one hour, but no pyelogram was seen at any time on either side. This was thought to be due to poor tubular function of the newborn child. Repeat subcutaneous pyelogram on Nov. 9, 1956, when the patient was 17 days old, showed a normal left kidney but nonvisualization on the right. It was the impression at this time that the patient had a Wilms's tumor or a congenital hydronephrosis and, since surgery was contemplated, no cytoscopy or retrograde pyelogram was carried out. Laboratory studies showed a red blood count of 4,210,000, a white blood count of 13,300, and a hemoglobin of 16 Gm. The urine had a specific gravity of 1.010 and tests for sugar and albumin were negative. Microscopic examination of the urine was also negative.

Exploration was carried out on Nov. 14, 1956, through a right lumbar incision. The mass was easily exposed and the pedicle allowed delivery through the wound so that it lay on the abdominal wall without tension (Fig. 1). Gross inspection of the tumor showed no evidence of renal tissue but rather a mass consisting of approximately thirty-six thin-walled cysts of similar size, closely adherent and attached by a common pedicle. This pedicle consisted of small vascular trunks and an apparent ureter, but no grossly discernible renal pelvis was present. These structures were clamped, ligated, and divided with subsequent removal of the tumor and closure of the wound in a routine fashion. The patency of the ureter was determined following the operation by injecting Renografin, 30 per cent, into the lumen and obtaining a roentgenogram of the specimen (Fig. 2).

Pathological Report.—The specimen was a 10 by 5.5 by 4 cm. multicystic structure which contained clear fluid. The multicystic spaces did not intercommunicate and a clear, pale, straw-colored fluid was found in each. The ureter appeared normal with the ureteral lumen measuring less than 0.5 mm. No pelvic cavity could be traced.

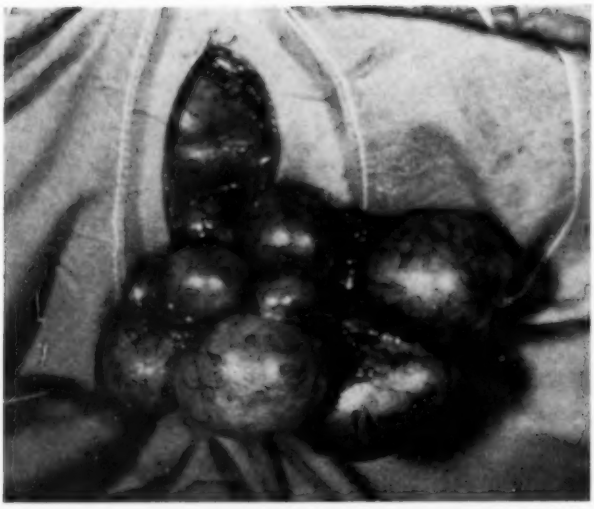

Fig. 1.—Exploration on the right revealed a typical multicystic kidney.

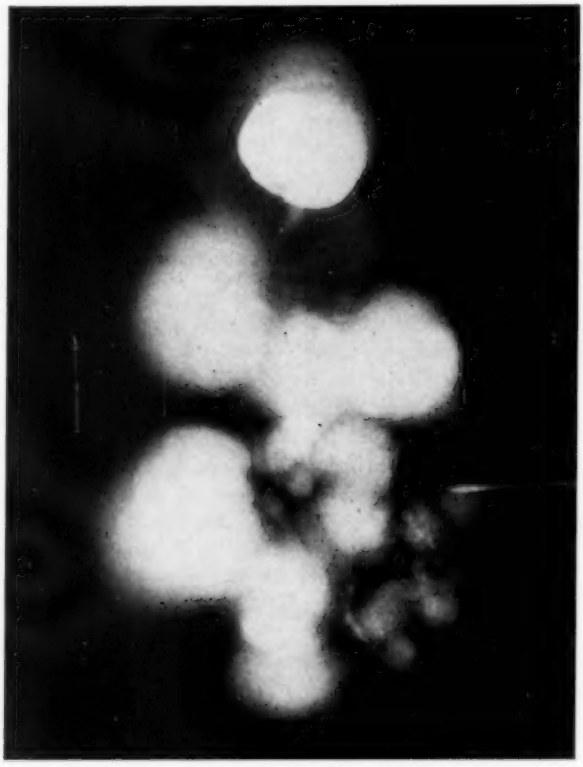

Fig. 2.—Injection of the ureter showed patency and communication with the cysts.

Microscopic Description.—Congenital polycystic kidney with elements suggestive of the so-called multicystic form with dilated, atrophic tubules and atrophic glomeruli surrounded by large amounts of collagenous tissue. In these areas the renal parenchyma was practically absent. This has also been designated as congenital unilateral multicystic kidney disease (Fig. 3).

The patient tolerated the procedure well and had an uneventful course, being discharged on the seventh postoperative day. He has been followed periodically since discharge and is in excellent health.

Fig. 3.—Photomicrograph showing dilated atrophic tubules surrounded by collagenous tissue.

Case 2.—V. I. W., No. 544525, was a 6-week-old female infant who was admitted to the University Hospital on March 28, 1944. The baby had been delivered spontaneously in another hospital after an uncomplicated labor. Nine days after birth she was found to have a "large abdomen." The parents were advised to bring the patient to the University Hospital for evaluation but instead took the infant home. Because of persistent vomiting which occurred after almost every feeding and failure to gain weight, the infant was finally brought to the hospital for treatment. Physical examination revealed a poorly nourished child with a large, smooth, movable, cystic mass which extended to the midline medially and to the posterior axillary line laterally, on the left. The remainder of the physical examination was negative. A subcutaneous pyelogram showed a normal right kidney with nonvisualization on the left and a large indefinite mass on this side. Upper gastrointestinal studies were normal except for evidence of an extrinsic mass on the left. The preoperative diagnosis was congenital hydronephrosis or a Wilms's tumor. Laboratory studies showed a red blood count of 5,800,000, a white blood count of 5,240, and a hemoglobin of 80 per cent. The nonprotein nitrogen was 25 mg. per cent. The urine was clear yellow with a 1+ albumin and 15 to 20 white blood cells. No red blood cells or bacteria were present.

Exploration was carried out on April 10, 1944, through a left lumbar incision. The

kidney was exposed and seemed to be made up of "multilocular cysts." One of these was opened and what appeared to be clear urine was seen to drain from the cyst. Nephrectomy was performed without incident and the wound closed in a routine fashion. No mention was made of the ureter or pelvis although it was requested that the ureter be carefully examined. The surgeon's postoperative diagnosis was "congenital cystic disease of the kidney."

Pathological report: The specimen was a multilocular kidney with no evidence of functional parenchyma. The multiple locules were independent of each other and there was no gross communication of these with the pelvis. (The specimen was not injected.) The calyces could not be definitely outlined. The ureter was very thin but showed no evidence of stenosis.

Microscopic description: There were multiple multilocular cysts which had a flattened mesothelial lining but no identifiable renal tissue was seen. The proximal ureter was normal in size and patent.

The patient had an uneventful hospital course and was discharged on the eleventh postoperative day.

This patient is now 14 years of age and is in excellent health.

DISCUSSION

Spence,[8] in his review of the subject in 1955, emphasized the features of unilateral multicystic kidney disease which warrant its classification as a separate entity. He felt that this condition should not be confused with multilocular cysts of the kidney, polycystic disease, solitary renal cyst, or multiple simple cysts of the kidney.

Multilocular cysts of the kidney may be distinguished from unilateral multicystic kidney disease by the fact that the cysts are limited to a portion of the kidney, leaving a normal segment uninvolved. Also the large cysts are subdivided and partitioned, with cysts within cysts being found. Similarly, otherwise normal kidneys containing a single solitary cyst or multiple simple cysts may be easily recognized.

Polycystic renal disease differs from the condition we are discussing in that the former is almost always bilateral and is also hereditary. In both the infantile and adult forms of polycystic disease the renal contour and calyceal pattern are retained grossly and the pelvis and ureter are usually normal. The microscopic sections show relatively normal-appearing nephrons, capable of function, interspersed among the cysts in contradistinction to the absence of functioning nephrons in the multicystic kidney. The differentiation between these two conditions is particularly important since with unilateral multicystic kidney disease the prognosis is quite favorable while with polycystic disease it is invariably fatal.

In reviewing the subject and the cases in the literature certain points are brought out which are of considerable interest and importance:

1. The condition is nearly always discovered in infancy or early childhood.

2. A palpable mass is frequently present.

3. Excretory urography shows nonvisualization of the kidney on the affected side and frequently evidence of a mass in the abdomen.

4. At cystoscopy the ureteral orifice on the affected side is often absent.

5. In some cases gastrointestinal symptoms leading to inanition are seen.

6. Nephrectomy results in cure of the condition.

7. Examination of the specimen grossly usually reveals no identifiable renal tissue and often an absent or atretic ureter.

Unilateral multicystic kidney and the articles pertaining to it were reviewed in 1955 by Spence[8] who reported 19 cases including his own. In addition, Lih and Waud,[9] in 1952, and Berman and Oweida,[10] in 1955, had each reported a case, which, although designated as a unilateral polycystic kidney was typical of unilateral multicystic kidney disease. Weinberg, O'Connor, and Senger[2] presented 3 cases in 1956 and since then there have been several additional case reports.[7, 11-14]

SUMMARY

Unilateral multicystic kidney disease is a congenital condition characterized by replacement of normal kidney tissue by multiple cysts of varying size held together loosely by connective tissue. The condition should not be confused with the other cystic lesions of the kidney and should be classified as a separate entity since it is apparently always unilateral and has a favorable prognosis. It is most often discovered early in life and should be considered in the differential diagnosis of an abdominal or flank mass in the newborn infant or child. The etiology of this condition is discussed and the previously reported cases are reviewed. The 2 cases presented bring the total to 31 recorded in the literature.

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AN EXPERIMENT IN TEACHING COMPREHENSIVE PEDIATRICS

DONALD C. ROSS, M.D.*
PHILADELPHIA, PA.

IN MANY centers of pediatric training, efforts are now being made to incorporate into the teaching program of the resident staff sufficient medical psychology and knowledge of psychotherapeutic techniques to enable the pediatrician to handle the emotional aspects of pediatric practice with awareness and skill.[1-5] By thus complementing the traditional pediatric training, it is hoped to turn out pediatricians who are capable of meeting the demands of modern practice at the beginning of practice. Previously pediatricians have had good training in the recognition and treatment of organic diseases, but much of their skill in handling the emotional aspects of practice has had to come from experience and has been acquired more intuitively than thoughtfully. Now that more than 50 per cent of pediatric practice has to do with the supervision of the well child's physical and mental health,[6] the interpersonal aspects of practice have become more and more important. The type of practice where the practitioner consciously brings skill to bear on both the organic and the emotional aspects has come to be known as comprehensive pediatrics.

The first pioneer in this field was Dr. Leo Kanner, who in 1932 published an account of the founding of the first psychiatric clinic in conjunction with a children's hospital at the Harriet Lane Home in Baltimore.[7] Over the next twenty years, more and more experience was acquired in many different centers in comprehensive pediatrics.[8-11] By 1952 this body of knowledge was sufficiently large that it was possible for the Committee on Child Psychiatry of the Group for Advancement of Psychiatry (GAP) to formulate and publish certain basic principles of teaching methodology,[12] which have since been further developed and elaborated by Rose.[3] The authors of the GAP report were careful to state that, while these basic principles were generally accepted, our knowledge was far from complete. It is realized that work in this field is still at an early stage of development, but it is now possible to approach the subject with the advantage of this organized body of knowledge.

Work in this area has also been underway in the adult field.[13-17]

During the two years, 1954 to 1956, the author was responsible for developing an experimental teaching program in comprehensive pediatrics

This experimental program was carried out in the Department of Neuropsychiatry, The Hospital for Sick Children, Toronto, Canada, headed by William A. Hawke, M.D., F.R.C.P. (Canada).

*Assistant Physician, Department of Child Psychiatry, The Children's Hospital of Philadelphia, Supervising Psychiatrist Philadelphia Child Guidance Clinic; formerly Staff Psychiatrist, The Hospital for Sick Children, Toronto, Canada. Present address: 1700 Bainbridge St., Philadelphia 46, Pa.

for the resident pediatric staff of the Hospital for Sick Children in Toronto, Canada, and utilized the principles enunciated by the GAP Committee on Child Psychiatry. This experiment therefore served as an opportunity for testing these principles in a pediatric setting which, because of its unusually large size, presented formidable problems in the organization of such a program.

The Hospital for Sick Children in Toronto has between 600 and 700 beds and is the principal pediatric resource in the Province of Ontario. It is primarily a service hospital, as the general hospitals in the Toronto area have few pediatric beds, and it therefore takes routine pediatric patients as well as those who require the special investigative and treatment facilities of a children's hospital. The bulk of the admissions to the medical wards are children with acute infections, and their hospital stay is short. The Hospital for Sick Children is also the pediatric teaching resource for the Faculty of Medicine of the University of Toronto, and the positions of Physician-in-Chief of the Hospital and Professor of Pediatrics at the University of Toronto are vested in one person. It is an active research center, the research being done under the auspices of the Research Institute of the Hospital for Sick Children, and this brings another influence to bear on ward practice. It is one of the most important training facilities for pediatricians and pediatric surgeons in Canada.

The Pediatric Service is divided into seven teams, each permanently headed by a senior pediatrician, and each has patients on the infant ward, preschool ward, and the ward for older children. One team has the infectious ward as its entire responsibility, and the other six teams have no responsibilities there.

A child guidance clinic was developed in connection with the pediatric outpatient department of the hospital by Hawke and Griffin in 1935. It has served both hospital patients and the usual child guidance patients from the community, who receive no other service from the hospital. The staff of this clinic has always provided a consultation and psychological testing service to hospital patients, and there has always been some informal discussion of patients with resident staff members during consultations. From time to time the staff of the clinic has presented emotional problems at clinical conferences and has given lectures to the resident staff. However, until this experimental program began, there was no organized teaching program of medical psychology adapted to meet the needs of pediatricians.

The goals of the program were to teach the resident staff to practice comprehensive pediatrics. I think they can be most succinctly described by quoting from the 1952 GAP Report.

> "Such practice would include constant alertness on the part of the pediatrician to the emotional implications of all he sees and does; understanding of the facets in the relationship between child and parent, between child and physician, and between parent and physician; the inclusion in histories of psychological data relevant to emotional development and to the problem at hand; knowledge of community resources and the ability to use them; the capacity to differentiate between problems which should continue to be handled by the pediatrician and those which should be referred to a child psychiatrist or elsewhere; and the ability to prepare properly both parent and child for such a referral. . . . The comprehensive pediatrician views parents

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as potential collaborators rather than as intruders, and much of his effort is directed at lessening the anxiety which is ever-present in both parents and child. For example, he so conducts routine procedures (such as venipuncture, physical examination and hospital admission) as to minimize their anxiety-producing potentialities. Knowledge of one's own emotional responses and the capacity to control them are essential for a feeling of security in this type of practice."

The basic means by which these goals were to be achieved were as follows:

1. The program would be supported by the medical staff, particularly by the Physician-in-Chief.

2. Psychiatric consultations would be a part of the program so that they could be used as a medium for instruction and not merely as diagnostic sessions with an outline of opinion and advice.

3. Direct individual supervision of the residents' cases would be the foundation stone of the program, and this would be compulsory to the same degree that ward rounds are compulsory, that is, that the resident would be expected to attend the supervisory meetings regularly.

The program was started in July, 1954, and the first six months were ones of preliminary experimentation in an effort to find the best way of implementing these principles within the realities present at the Hospital for Sick Children. One of the most serious realities was the limitation of time. The resident staff already had many calls upon their time, and the author had responsibilities in the child guidance clinic, so that there were only three half-days a week assigned to this project. He was, however, in the hospital eight half-days a week, and made himself as available as possible to the residents during this entire time, if not personally, then by telephone.

The resident staff consisted of: a chief resident, an assistant chief resident, six senior interns taking their second year of pediatric training, fourteen junior interns who had previously completed a rotating internship and who were taking their first year of pediatric training, two interns who had previously had a rotating internship and were taking a two-year general practitioner's course, rotating through several hospitals and spending four months on pediatrics, and two general rotating interns who were rotating from general hospitals for a month's experience in pediatrics as part of their general rotating internship. It was obviously impossible, in the time available, to reach the entire resident staff on any regular individual basis, and so a great deal of thought went into the problem of who should be reached and when.

It was finally decided to concentrate on the group of residents who were taking their first year of pediatric training and to see each of them once every two weeks throughout the entire year, regardless of what team they were on. It was found that if they were only seen during their rotation on one or two of the ward teams, the advantages of having the individual supervisory conferences on a more or less compulsory basis were nullified by the fact that if the intern was not immediately interested in the program he could readily avoid it, on one pretext or another, if his association with it was only over a period of a few weeks. It was found that this did not allow sufficient time for the intern's

interest to be stimulated and for him to develop enough skill to begin to find the new approach rewarding.

Those taking their second year of pediatric training were omitted as there was not sufficient time available to work with both groups on an individual basis, and this group was not, for the most part, immediately responsible for patients, nor were they taking histories or having much direct contact with parents. Their role was more supervisory and consultative to the juniors, and after some trial interviews with them it was decided that, in order for it to have much meaning for them, the focus of the program would have to be the problems they encountered in their supervisory and consultative capacity to the juniors. However, consultations were available to this group and to all interns in the hospital, medical and surgical, on request. Also counseling interviews, as many as were required, were offered through the chief resident to any medical intern who was having difficulties in the interpersonal aspect of his work with patients or colleagues.

Group meetings were attempted during the experimentation of the first six months in an effort to provide an opportunity to discuss, from case material, the more subtle signs and symptoms of emotional disturbance, so that the interns could better recognize the emotional problems they encountered. It was found, however, that the case material available contained insufficient psychological data to make this approach rewarding, and so these meetings were omitted, and the entire effort was focused on an individual approach to the first year group of interns.

Psychiatric consultations were concentrated upon as a means of increasing the intern's knowledge of psychodynamics and as an opportunity to improve his interviewing technique. When an intern requested consultation, he telephoned the psychiatrist's secretary and arranged a time when the psychiatrist, the parent, and he could meet together to try to understand the emotional aspects of the case. These interviews stimulated much interest and were found to be the most valuable part of the program because in them the intern had the opportunity of seeing his own case laid open so that the emotional problems involved were understood and were apparent to him from his own observations. At first the psychiatrist did most of the interviewing, but as the interns became more confident they often took over much of the interview and the psychiatrist participated only when he thought something was being overlooked, or when the intern seemed to want some assistance from him. It was during these interviews and the discussions of them which followed that most of the interns developed a student-teacher relationship with the psychiatrist. Following the interview the psychiatrist had a typed report prepared of his understanding of the case, written in simple, nontechnical language; this was put on the chart and copies were sent to all physicians interested in the case and to all personnel working with the child, such as the head nurse, the occupational therapist, the recreation worker, the public health nurse, etc. These psychiatric consultation reports were found to be an extremely effective way of overcoming the formidable problems of communication in a large hospital,

and a number of the attending medical staff commented favorably upon them as they seemed to present the psychodynamics of the case in a way that they found interesting and useful.

Greenhill and Kilgore,[15] in their excellent account of their experience with a similar type of compulsory program with medical house officers on a medical service at Duke University's School of Medicine, discuss at length the resistance encountered in the house officers, and state: "Under the plan of organization used in this study, the resistance of the medical house officer to the psychiatric approach was the major obstacle to instruction. The methodology in teaching the approach narrowed down mainly to dealing with this resistance." They go on to classify the resistance they encountered into seven different categories and describe elaborate techniques for dealing with it, such as challenging in conference the house officer who was suspected of developing increased resistance, and then sending one of the group after him following the conference to encourage him "to ventilate" his feelings. No such manipulatory techniques were utilized in this program, although resistances were discussed quite openly with interns when it was apparent that these resistances were interfering with the care of patients or the quality of histories. It was the author's experience also that the resistance to the program was the major problem encountered.

Much of the initial resistance seemed to be the result of the intern's inability to comprehend the goals of the program. It was commonplace in the final interview for the intern to recommend that in future the program be explained in more detail at the beginning, because, if he had understood what it was about sooner, he would have been less resistant and would have made progress earlier. When he was reminded that this had been done, that an hour had been spent at the beginning discussing the goals of the program with him alone, and that he had been asked if there was anything that he did not understand, he would agree that such had been the case, but say that for some reason he had thought he had understood it but actually had not. None of the interns could say why this was, but it was the author's opinion that it was because the program involved concepts which up to that time were outside their experience. For example, the concept that in skillful interviewing it is as important to be aware of the feelings being communicated as it is to be aware of the facts being given, and that as much valuable and pertinent information is often communicated by the feeling tones as by the facts, is hard to appreciate fully until observed with the assistance of an experienced interviewer. This opens up a new dimension for the intern in his interviews, and it is only after some experience with it that its full scope is realized. Another unrealized concept is that strong feelings in the parent, such as anxiety and anger, can block the giving of a good history unless the interviewer utilizes certain psychotherapeutic techniques to reduce the intensity of these feelings. Where these blocking feelings are expressed by withdrawal and monosyllabic replies on the part of the parent, the intern tends to feel frustrated by the lack of emotional connection he makes with the parent,

and he diagnoses the parent as "stupid" and gives up, or becomes hostile himself, which reinforces the parent's hostility or anxiety and makes good histories even more difficult to obtain. After these techniques were observed in action, the intern's motivation for sharpening his perception of communicated feelings and for developing skill in using psychotherapeutic techniques was frequently aroused. This type of resistance based on lack of understanding and skepticism was observed with all the interns and was considered normal, and for this reason the compulsory nature of the program was most valuable for it served the purpose of having them persist with the program until a better understanding began to develop through first-hand experience.

The practice of having the psychiatrist's relationship with each intern as individualized as possible and geared as much as possible to his particular needs and tolerances was the first principle of the methodology of handling resistance. Some interns felt uncomfortable coming to the psychiatrist's office, and with them the interviews were held in small offices off the wards. The interviews were always kept geared to the intern's patients, and when he said that he had no patients with emotional problems the psychiatrist would suggest that they make rounds together. Sometimes there would be no appropriate material, but at other times there would be cases where there were important problems to be handled, but ones that had not been recognized because of the intern's lack of experience. As there was often insufficient material about the emotional aspects of the case on the chart for a full understanding of the problem, it was usually suggested that the intern and psychiatrist interview the parents together. These ward rounds, therefore, served as an important method of teaching the interns the significance of material that indicated emotional disturbances which might have a bearing on the total management of the cases. With those interns who were using the excuse of "no cases" as an evasive tactic, the ward rounds often turned up cases with the grossest type of emotional disturbances which were prime factors in management, and about which they had done nothing. A discussion of the omission would bring forth a grudging admission of its importance, but result in further evasive tactics, such as not responding to his call at the time of the interview with the parents and psychiatrist, etc. It is the author's opinion that the intern with this type of obvious problem in taking responsibility, not just in this kind of program but in his duties generally, can only be reached by an evaluation with those responsible for the over-all pediatric training program.

Twenty-two junior interns were involved for a sufficient length of time for some opinion to be formed about their attitude to the program and the use they made of it.

Use was construed in the most modest terms, requiring only that the intern was sincerely trying to practice comprehensive pediatrics and that he had conviction that behind such symptoms as functional enuresis, functional soiling, and functional abdominal pain there lay emotional problems, usually involving the parent-child relationship, that could be understood through the use of interviewing techniques that

could be learned. It was realized that none of the interns who completed the program would be consistently capable of handling even relatively minor emotional difficulties in their patients, but it was hoped that when they had not handled a case well they would be aware of it and would reflect upon how they could have done it better.

After each interview with an intern the salient points of the interview were dictated, and this dictation was examined in coming to an evaluatory opinion. In the final interview the intern was asked for his reactions to the program, and whether or not he had found it of value in improving his own practice, and this opinion was considered in the evaluation. As would be expected, the ones who made use of the program were the ones who felt it had been valuable. For the purpose of estimating the use the interns made of the program, they were divided into four groups.

Group I contained those who made most use of it. There were six in this group, three men and three women. They became actively involved with the program and would request assistance with the emotional problems of their cases and invest time and effort in dealing with them. They were people with a great deal of compassion and understanding.

Group II was a more heterogenous group consisting of eight interns, four men and four women, all of whom, in the end, were kindly disposed and receptive to the program, and participated in it, but for a variety of reasons did so less fully than those in Group I. For example, one intern, who will be discussed later, was rated in this group because he had revised his attitude to patient care much more than some of those who were more geared to a comprehensive approach from the beginning and used the program to refine their techniques rather than modify their attitudes.

Group III was less interested than either of the first two groups, but its members did participate, and discuss cases with the psychiatrist, and genuinely involve themselves at least to some degree. There were three in this group, two men and one woman.

Group IV was made up of confirmed resisters, and their resistance was both intense and inaccessible. There were five in this group, and all of them were men. Two resisted openly and three passively, paying lip service to the value of the program, but involving themselves in it as little as possible.

For purposes of comparison the same twenty-two interns were divided into four groups according to the quality of their over-all work based on opinions that the child psychiatrist obtained from members of the medical staff, the chief residents, head nurses, etc.

Group I was made up of interns who were efficient, conscientious, did excellent work, and were sincerely interested in their patients. There were eight in this group, five men and three women.

Group II was made up of the interns who did good all-round work, but had less intense interest and enthusiasm than the first group. There were five interns in this group, two men and three women.

Group III was made up of interns whose work tended on the whole to be no better than average. There were six interns in this group, four men and two women.

Group IV was made up of those interns who were having gross difficulties because of inability to carry responsibility or because of indecisiveness of such a degree as to seriously interfere with their work, or both. There were three interns in the group, and all of them were men.

TABLE I. COMPARISON OF INTERNS' USE OF PROGRAM WITH QUALITY OF OVER-ALL WORK

INTERN	SEX	GROUP RATING ON USE OF PROGRAM	GROUP RATING ON QUALITY OF OVER-ALL WORK
1	M	II	III
2	F	I	I
3	M	III	III
4	F	II	III
5	F	II	II
6	M	III	II
7	M	IV	IV
8	M	I	I
9	F	III	III
10	F	II	I
11	F	II	II
12	M	II	II
13	M	IV	IV
14	M	IV	III
15	F	I	I
16	M	IV	III
17	F	I	II
18	M	III	I
19	M	I	I
20	M	I	I
21	M	IV	IV
22	M	II	I

The association between the ratings of the two scales was determined in order to see if a significant relationship existed between the use the twenty-two interns made of the program and the over-all quality of their work. It was realized that even if such a relationship should exist, because of the small group involved and the crude criteria used it could be no more than a rough indicator. Since each scale has four steps, the frequency of agreement between the scales on the basis of chance alone would be 25 per cent, or 5.5 cases of the 22 interns. Actually, full agreement was obtained in 13 of 22 cases. The chi-square test[18] was used to examine the deviation of the obtained number of agreements from chance expectancy. With chi-square = 13.64 ($P < .001$) the minimum requirements for significance are more than met. It should, however, be borne in mind that the ratings may be contaminated by an unknown amount of "halo effect" because both ratings were made by a single judge, the child psychiatrist. Ideally, the ratings for the quality of over-all work should have been made by an independent judge who did not know how the interns were rated for the use of the program. To do this it would be necessary for all the criteria to be decided on in advance, and such a project could only be set up after the preliminary work described in this paper had been completed. However, the correlation demonstrated by the chi-square test between good use of the program and over-all excellence, and poor use of the program and less than adequate over-all performance, suggests a relationship worthy of further study.

The interns who did the best overall work seemed to be the ones who were most strongly motivated by a genuine interest in their patients and therefore were the ones who saw the most value in a comprehensive approach. It is noteworthy that most of the women interns seemed to fit into this category and seemed much more geared to patient care than professional advancement. One might speculate that their choice of pediatries as a specialty is a sublimation of the maternal role. None of them, even those with obvious problems in interpersonal relations, were deeply hostile to the program in the way that some of the men were, and all saw value in such goals as supporting the parents to support the child through the hospital experience, etc.

On the other hand, those interns whose major concern was the impression they were creating with their superiors tended to resent the program and avoid it, as it made for a further large and difficult area in which they felt they had to create a good impression. They also were the ones most sensitive to any cues that indicated skepticism on the part of members of the attending medical staff. One intern who fell into this category made absolutely no use of the program and learned nothing from it, but kept enthusiastically looking for cases that would be interesting to the psychiatrist. This pattern persisted regardless of how many times it was pointed out to him that the purpose of the program was to help him better handle his own practice.

In general, the men who made least use of it were the ones who tended to be most insecure in their work. In two instances there were obvious difficulties in assuming responsibility which showed up in consistent overt omissions in patient care. These interns were extremely threatened by the program and were fearful that it would expose their weaknesses. In the competitive atmosphere of a teaching hospital, it was virtually impossible for them to see the assistance available to them as supportive and constructive because they did not feel they could afford to admit the problem, much less work toward a solution. Instead, the more obvious the problem became, the more anxious they became, and the more they resorted to such defensive tactics as evasion, attack, etc. However, even here, it was the author's feeling that at least some of these men might be reached if the competitive attitude normally present in such a situation could be minimized. In such an atmosphere the intern would, hopefully, feel it was safe to admit such a problem and do something more constructive about it than expend his energy on efforts to conceal it.

The intern referred to previously, who was rated in Group II for his use of the program, was an exceedingly anxious intern who complained bitterly about not being given sufficient responsibility, but was obviously neglecting to fulfill responsibilities that he already had. He was, in the beginning, exceedingly hostile to the program, but in the end made quite good use of it and regretted that he had not done so earlier. In this instance, the psychiatrist, knowing that the intern was threatened by an examination of his handling of the interpersonal aspects of a case, for a time discussed cases that were known to them both, but were ones for which the intern

had no responsibility. Gradually he became less defensive and voluntarily began to ask for assistance in some of his own cases.

Three interns took advantage of the counseling service described earlier.

In their individual evaluation of the program a number of the interns said that they thought a few didactic orientating group meetings at the beginning on such subjects as social work, psychological testing, and community resources would have been helpful, and the author is in agreement with this recommendation.

In an effort to see if the program had had any effect on history taking, a dozen histories taken toward the end of the training year of each of the interns who were considered to have made best use of the program were selected at random and were examined and compared with histories of those who were felt to have made poor use of it. It was found that the program had not appreciably influenced routine history taking. The bulk of the histories examined were of children with some complication of an acute infection, and there was a highly stereotyped way of recording these, so that while they covered the important facts about the illness, they lacked individuality. It is true that many of these routine histories were undoubtedly of children who had no serious emotional difficulties. However, a positive statement that indicated that the intern had at least considered the emotional aspects of the case would seem desirable in these instances, but would, I think, only be recorded routinely if there were a special place on the printed history form for it.

The interns interested in comprehensive pediatrics, while they did not change their routine methods of recording histories, were on the alert for emotional problems and went more fully into selected cases where they thought a problem was present, and these were the ones they had brought for consultations. One history was found, taken by the intern mentioned above who had had so much difficulty with the program at first, in which he had carefully recorded a great many details about a child's adjustment and his relationship with his parents in a case of fecal incontinence which he considered to be on an emotional basis. Physical investigation proved to be negative, and the child was referred for psychiatric treatment.

It was the opinion of the social worker in charge of applications in the child guidance clinic that the quality of the referrals made to the clinic by the interns definitely improved in the latter part of each training year. The parents came with a better understanding of the child's condition, in both its physical and emotional aspects, and the relationship between these if there was one, and with a better understanding of psychiatric treatment and what they could expect from it.

The results of the experiment would indicate that the principles laid down by the GAP Committee on Child Psychiatry are sound, providing they are adapted to the needs of the particular institution in which they are being applied. In this instance the child psychiatrist was also a pediatrician, and this was felt to be a distinct advantage from the point of view of ease of communication with pediatricians.

It was obvious, however, from the two years' experience that in order for such a program to be fully successful in any hospital, comprehensive pediatric practice would have to become an established policy of the hospital because administrative changes would be required in such areas as admitting procedures, visiting, resident case loads, and continuity in patient care, with as few changes of interns on a case as possible. There is no doubt that if an intern is going to practice comprehensive pediatrics, and involve parents and work with them, it is going to require more of his time than it would under a system where parents are more or less excluded and only the physical aspects of the illness are considered. This does, however, seem to be only one aspect of the mounting cost of patient care as more and more of the complexities of illness are understood and methods are devised for investigating them and dealing with them, and it is a problem that will probably have to be solved by new approaches to hospital financing. Likewise a pediatrician trained in comprehensive pediatrics going into private practice will have to revise his thinking about what constitutes service, and will have to be compensated for time spent with parents on a scale proportionate to the time involved.

As medical schools incorporate training in medical psychology and psychotherapeutic techniques into their undergraduate psychiatric training programs, hospital programs like this one should go more smoothly, meet less resistance, and require a smaller proportion of time be spent on elementary concepts.

Also, to be fully successful, not only the concept that a physician's attitudes to parents and patient care can be a force for good or evil will have to be accepted as a fact, but also the corollary concept that it is his responsibility to do everything possible to modify unconstructive attitudes. This was a concept that met much resistance, because, while it was generally accepted in principle, in practice it was often construed as an infringement on the rights of the individual intern and a trespassing on his personal life. The point was frequently made by the child psychiatrist that he had no interest in the intern's personality organization except where it affected patient care, and, after the stage of initial resistance, this was mainly a contentious point only with the interns in Group IV (Use of Program) and with one intern in Group III (Use of Program). The majority of interns agreed that if, without being aware of it, they were doing something that was detrimental to their patients, they would welcome its being drawn to their attention. However, those who were most vocal about the program being an infringement on personal rights did at times mobilize considerable support for their point of view, and this strengthened their determination to ignore the emotional aspects of their practices.

The Nursing Service of the Hospital was a strong, well-organized one with its own training school. The attitude of the nurses toward a comprehensive approach to patient care was sympathetic, and their attitude toward the intern program in comprehensive pediatrics was very supportive. The individual nurses would frequently draw to the intern's attention emotional problems that they had noted

in patients or parents, and they were always willing to participate in ward conferences on particular patients and made valuable contributions at these conferences.

A word should be said about the value of a good department of social work, in which the social workers are trained in casework techniques, in conjunction with such a program. Once the intern has worked with the parents to the point of understanding the problem, and has realized that certain parental attitudes toward the hospital or the child's illness need modification, he can refer them to the social worker for casework help which can be of great value.

A psychological testing service is also necessary, but it was found that the information to be obtained from psychological tests and the limitations of these tests were frequently not understood by the interns. There was a tendency to request psychological tests when what was wanted was the assistance that could come only from a psychiatric consultation, and the policy was therefore adopted that all requests for psychological tests be cleared through the psychiatrist.

The time spent on this experimental project was often hectic, but was enjoyable because of the close contact it brought with young physicians, the problems they were experiencing, and the opportunity it gave at times to be helpful to them.

SUMMARY

1. An experimental program in teaching comprehensive pediatrics to first year pediatric interns in a large children's hospital is described, including the difficulties and resistances encountered, and the methodology of dealing with them.

2. The teaching was done on an individual basis with the interns having regular appointments with the child psychiatrist, and these meetings were compulsory to the extent that ward rounds were compulsory in that the physician-in-chief expected the interns to attend.

3. The collected data indicate that there may be a correlation between quality of over-all work and willingness to participate in such a program, and that this is a relationship worthy of further study.

4. The program was based on the principles laid down by the Committee of Child Psychiatry of the Group for Advancement of Psychiatry, and these principles would seem to work well providing they are adapted to the individual setting.

The author gratefully acknowledges the valuable assistance of Elaine Dorfman, Ph.D., with the statistical analysis of the material.

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Clinical Pathological Conference

THE CHILDREN'S MEDICAL CENTER

BOSTON, MASS.

SIDNEY FARBER, EDITOR

JOHN M. CRAIG, ASSISTANT EDITOR

AT THE age of 4¼ years, this boy began to have short episodes of abdominal pain and fever. When bone pain, hepatosplenomegaly, and lymphadenopathy were noticed, two months later, blood studies revealed a hemoglobin of 11.0 Gm. per cent and a leukocyte count of 11.6 thousand per cubic millimeter, with a differential count of polymorphonuclear cells 13, band forms 4, and lymphocytes 83 per cent. A smear of the sternal marrow was interpreted as displaying a predominance of lymphocytes, and an inguinal lymph node biopsy was diagnosed as lymphosarcoma.

On admission to the Tumor Therapy Service at The Children's Medical Center, the child was acutely ill, with a temperature of 104° F., and he displayed pallor, generalized lymphadenopathy, hepatomegaly of 7.0 cm., and splenomegaly of 12.0 cm. The neurological examination was negative.

The admission laboratory examination gave the following results: hemoglobin 7.9 Gm. per cent, leukocytes 1.7 and platelets 3.0 thousand per cubic millimeter. The differential count was: polymorphonuclear cells 14, band forms 14, young lymphs 8, and adult lymphocytes 64 per cent. The sternal bone marrow aspirate contained 94.6 per cent blast forms. A diagnosis of acute leukemia was made.

The patient was given a transfusion, and antileukemic therapy with Methotrexate, 5.0, and cortisone, 150 mg. per day, was initiated. Erythromycin and chloramphenicol were given in anticipation of a positive blood culture. This, however, turned out to be negative, and the child became afebrile on the third day. He was discharged, improved, on the seventh day of hospitalization.

A month after the first admission, the peripheral blood studies gave normal results, and a bone marrow aspiration revealed a normal distribution of cells with only 3.1 per cent blast forms. Cortisone was discontinued and Methotrexate was decreased to 2.5 mg. per day and then, later, to every other day.

Two weeks later, he began to vomit daily and was found to have marked bilateral papilledema. A lumbar puncture yielded clear fluid under a pressure of 450 mm. of water, containing 450 mononuclear (blast?) cells per cubic millimeter. Skull films showed separation of the sagittal and coronal sutures. Electroencephalogram revealed an occipital asymmetry with low

voltage on the left. Chemotherapy was changed to 6-mercaptopurine, 50 mg. per day. Also, roentgen therapy was directed to the right and left lateral skull parts for a total depth dose of 963 roentgens over a period of seventeen days. At the end of the therapy period, the papilledema had subsided, the cranial diastasis had not increased, and the child was clinically well.

A bone marrow aspiration six weeks after the onset of cerebral symptoms showed a normal complement of cells with 2.0 per cent blast forms.

Three months after his first admission, lethargy and vomiting recurred intermittently. One month and a half later, hemoglobin was 8.1 Gm. per cent, leukocytes 2.1, and platelets 122 thousand per cubic millimeter. The differential count was: blast forms 2, band forms 25, polymorphonuclear cells 26, myelocytes 1, eosinophils 1, lymphocytes 40, and monocytes 5 per cent. Chemotherapy was changed to prednisone, 40 mg. daily. Over the next two months the hemoglobin fell to 5.2 Gm. per cent, the leukocytes to 0.7, and the platelets to 42 thousand per cubic millimeter. Methotrexate was again given, 2.5 mg. per day. Pharyngeal and oral moniliases were noted and effectively treated with nystatin, chloramphenicol, erythromycin, and sulfisoxazole.

His second admission took place seven months after his first because of right-sided headache for three days and a left hemiparesis for one day. At this time the vital signs were normal though the patient was pale, alert, and irritable. There was a complete left hemiparesis including the facial muscles. Cracked-pot percussion sounds were elicited over the head. A diminished pupillary reflex with lateral nystagmus was found on the left, and a mild degree of papilledema was noted on the right. The deep tendon reflexes were hyperactive and a positive Babinski was present on the left.

The hemoglobin was 6.7 Gm. per cent, the leukocytes 4.5, and platelets 4.0 thousand per cubic millimeter. The differential count was: band forms 7, polymorphonuclear cells 28, metamyelocytes 5, and lymphocytes 60 per cent. The cerebrospinal fluid pressure was 190 initially, falling to 125 mm. of water; the fluid contained 143 mg. per cent protein, and 66 of sugar. The cells were: 61 leukocytes per cubic millimeter, with 57 monocytes and 4 polymorphonuclear cells; a culture was negative. Repeated taps, 3 and 18 days later, gave protein contents of 254 and 145 mg. per cent, respectively. The cellular content was unchanged, as were also the electroencephalograms and the skull roentgenograms. On examination, the bone marrow was hypoplastic, with a predominance of lymphocytes; 5 per cent of the cells were blast forms.

The child was febrile, with temperatures swinging to 102° F., throughout his hospital stay. No infectious agent was isolated, but antimicrobial therapy was nevertheless continued, at first with nystatin and chloramphenicol. This was changed later to penicillin and streptomycin during the last four days in the hospital. Methotrexate was discontinued because of the marrow hypoplasia. He received a second course of radiation to the head totaling 800 roentgens over 8 days. After 17 days the child was discharged unimproved, only to return 2 days later with more lethargy. He now required gavage feedings, and began to have generalized twitching, uncontrolled by

intravenous barbiturates. Terminally hypotension was noted. He died three days after his last admission, at the age of 5½ years, some ten months after the onset of his first symptoms.

DISCUSSION

DR. BENJAMIN ALEXANDER.*—There was a great preponderance of blasts in the bone marrow taken after admission to The Children's Medical Center, and a diagnosis of acute leukemia was made. I think you will all agree that this was made more on the basis of pathologic findings in the bone marrow than on evidence of leukemic involvement in the peripheral blood. One would put this, as a clinical diagnosis, into the category of acute aleukemic leukemia. Lymphosarcoma, I think, represents a preferable diagnosis because there is no evidence of involvement of the blood other than the pancytopenia, which is a negative form of evidence. The patient was given a transfusion, I presume because of the thrombocytopenia, although one wonders if he had hemorrhagic phenomena. I would venture to say that he did, with this degree of thrombocytopenia.

I would be curious to know how many transfusions were used in this child's management—not that I think they would account for the favorable turn of events. Dr. Toch, are there any data pertaining to that?

DR. RUDOLF TOCH.—One single transfusion was given.

DR. ALEXANDER.—I am also curious to know if there were any abnormal findings by x-ray in the chest. The reason I ask this is because we are confronted with an intracranial complication, and we know that certain intrathoracic pathologic conditions frequently metastasize to the brain. Is there any evidence of pulmonary involvement, Dr. Toch?

DR. TOCH.—The lungs were negative.

DR. ALEXANDER.—One would also want to know whether the peripheral blood was also essentially normal throughout the period of the apparent five-month remission. I would like to know that because, as I said, the intracranial complication took place during this period. This is the cardinal point in this case—whether this complication took place at a time when the underlying disorder seemed to be well under control. Also, the nature of the complication is obscure. Therefore, I would like to know if the child had anemia, normal platelets, or hemorrhages, and whether there was any trauma.

DR. TOCH.—The peripheral blood was essentially normal in this period. To give an example, on one occasion the leukocytes numbered 7,100 per cubic millimeter, the hemoglobin was 12.1 Gm. per cent, the platelets were 310,000 per cubic millimeter, and the differential was: bands 1, polys 48, eosinophils 1, lymphocytes 42, and monocytes 50 per cent. This was quite representative of this whole period.

DR. ALEXANDER.—When he began to show bilateral papilledema after exhibiting the clinical phenomena of vomiting, which is undoubtedly related to the increase in intracranial pressure, the Methotrexate was discontinued and the child was put on mercaptopurine in substantial dose. The thinking of the clinicians at this time

*Dr. Benjamin Alexander is Associate Professor of Medicine, Harvard Medical School, at the Beth Israel Hospital, and Consultant in Medicine, The Children's Medical Center.

was that the child was no longer responding well to the antifolic acid derivatives, and accordingly should be shifted to another agent which operates via a different mechanism. A lumbar puncture and x-ray at this time confirmed the clinical evidence of increased intracranial pressure. There were also cellular elements, presumably blast forms, in the cerebrospinal fluid. We have no evidence in this record to indicate that this intracranial complication was directly related to the underlying disorder, namely, lymphomatous infiltrations, or whether it was due to hemorrhage, infection, or, for that matter, to a totally new primary malignancy, unrelated to the original. The attending physician, however, recognized the probability of a complication of the underlying lymphosarcoma and, accordingly, invoked local x-ray therapy. This apparently was followed by substantial clinical improvement.

A lymphosarcomatous infiltration could well have responded to x-irradiation. Similarly, a medulloblastoma would also have been responsive, but other forms of intracranial neoplasm are generally not favorably affected.

The neurologic complications of leukemia or lymphosarcoma are well known. They occur in 10 to 20 per cent of cases, generally involving the peripheral nerves, rarely the spinal cord (except when the skeletal system is compromised by spontaneous compression fractures of the vertebrae). Cerebral infiltration by leukemic cells may occur as any tissue of the body might become infiltrated, but it is one of the less commonly encountered complications in adults, although there may be a general widespread infiltration. Localizing lesions giving rise to hemiplegia are uncommon. On the other hand, hemorrhage is a common complication of lymphosarcoma, usually secondary to the thrombocytopenia. It should be borne in mind, however, that other disturbances in coagulation may occur in leukemia, particularly deficiency of AC globulin, the labile factor in plasma essential for the prothrombin conversion mechanism. If severe enough, such a defect might make its first appearance clinically in the form of hemorrhage, or, if not very severe, in the form of an elevated prothrombin time (retarded prothrombin conversion). Dr. Toch, I would like to know whether or not this child showed hemorrhagic phenomena?

DR. TOCH.—There was no evidence of bleeding at all.

DR. ALEXANDER.—After a fairly long interval with a deteriorating blood picture, he was admitted with an acute localizing lesion involving the right side of the head with left hemiparesis, and, later, involvement of one of the cranial nerves. The cerebrospinal fluid had a normal sugar level, and no growth was obtained on culture, which helps exclude a bacterial agent as underlying the intracerebral condition. The cerebrospinal fluid protein was quite high, with xanthochromia, which indicates red cell accumulation either close to the meninges or free in the subarachnoid space, though there was never any evidence of free blood in the subarachnoid space.

We find that the bone marrow was now very hypocellular, with the preponderant cells being lymphocytes, with 5 per cent blasts. I would be curious to know what the other cells were.

DR. TOCH.—The bone marrow aspiration differential was: immature granulocytes 15, mature granulocytes 13.6, erythroid cells 23, and lymphocytes 42 per cent.

DR. ALEXANDER.—I have always been interested in what possible epidemiologic factors might be uncovered in leukemia. I am very much impressed with the increased usage of organic solvents as a consequence of chemical industrialization of our country, as well as of Great Britain. On inspection of the statistics for leukemia over the past three decades, one is impressed with the direct linear increase in morbidity and mortality from leukemia, which in a way parallels the great chemical industrialization going on here and abroad. On the other hand, there have been very recent data in the British literature regarding the high incidence of leukemia in children of mothers who had received extensive x-ray studies during the late gestational period.

Accordingly, is there any knowledge regarding possible exposure of the mother of our patient to x-irradiation or chemicals in connection with her pregnancy?

DR. TOCH.—There was no x-ray or unusual chemical exposure.

DR. ALEXANDER.—Now, we are left with a diagnosis of lymphosarcoma or acute lymphatic leukemia, which I think is an entirely tenable diagnosis from all the information we have at hand. The cardinal question now comes up regarding the cerebral complication, in view of the fact that this child was under good therapeutic control. In considering that, we have to think in terms of possible infiltration or localizing of lymphosarcomatous tumor in the right parietal-occipital region, or, indeed, of an independent neoplastic disease. The most common independent neoplasms encountered in leukemias, as far as I have been able to ascertain, are those of skin, lip, and stomach—in that order. Multiple neoplastic disease in individuals is not an uncommon occurrence. This cerebral process is most likely not a hemorrhage. Yet hemorrhagic complications in leukemia are certainly common. One would not consider such a complication seriously because the platelets were normal, and there were no other clinical hemorrhagic phenomena.

Also, we find no support for an infectious lesion. Moreover, this child's neurological complication apparently responded to localized radiation, so that I would have to say that, while many possibilities are considered, we are left with the probability that this cerebral complication was associated with his underlying disease, which is acute leukemia or lymphosarcoma, and that this occurred in the face of good control of the peripheral blood and marrow leukemic processes. It is perfectly possible that whereas the bone marrow in other parts of the body could very well be susceptible to, and controlled by, the antifolic derivatives and other antileukemic agents, this might not occur in the central nervous system because the blood-brain barrier might not be passable by such drugs as were used. This then could explain the persistence of neoplastic cells and the subsequent development of an intracranial complication responding to radiation, once these cells had spread to the brain.

DR. FARBER.—Thank you, Dr. Alexander.

Dr. Byers, would you offer an opinion concerning the nature of the changes in the electroencephalogram?

DR. RANDOLPH K. BYERS.—The tracing shows a general diffuse rate of about 4 to 5 per second with a quite symmetrical slowing in the right and left occipital region. I would think that this diffuse slowing was due, possibly, to intracranial pressure or to some destructive lesion in the brain stem, which lowered the general activity. This also, of course, suggests a lesion of the occipital cortex or the forebrain. The point of damage cannot be determined from this tracing, but with the left hemiplegia the answer becomes more obvious.

When I saw this boy earlier, there was one other thing that had to be considered. This was a peripheral neuritis, such as Denny-Brown has reported in the presence of neoplasms[1]; I believe we have seen other similar cases in children in the Tumor Therapy Clinic, whose leukemia is in remission. The explanation that Dr. Alexander has given is probably the correct one—that the antileukemia drug is able to control the neoplastic process outside the blood-brain barrier, but inside the blood-brain barrier it may not be effective.

The thing about this child that was a little different was that he did not have an increased intracranial pressure when he died; this had been relieved by treatment. When I saw him before death, he had functional defects, but no increase in cerebrospinal fluid pressure, and I thought his brain stem was transected by neoplastic infiltration.

DR. FARBER.—Dr. Toch, would you summarize our experience, briefly, on the blood-brain barrier problems as seen in the leukemic patient?

DR. RUDOLF TOCH.—We have seen, in the past four years, a good number of children who have had increased intracranial pressure, characterized clinically at first by vomiting and headache, and later by drowsiness. The eye grounds show papilledema, the x-rays splitting the sutures, and the lumbar puncture an increased cerebrospinal fluid pressure. For those who wonder whether we were not foolhardy in doing a lumbar puncture in the presence of papilledema and high pressure, we did it with neurosurgical sanction, and very carefully. We have believed that inability of the drugs to cross the blood-brain barrier must be the problem, because only those children who were on antimetabolites have developed this problem. Children who have received adrenal steroids have not shown increases in intracranial pressure. Whether or not that will be borne out as we have had more experience, I do not know, but it is so for the moment.

At the moment, we use two approaches to therapy. X-ray therapy to the brain has been effective and convenient, but it has the disadvantage of causing alopecia. We have, in a few instances, given intrathecal Methotrexate in amounts of 1 to 2 mg. every day or every other day for three or four doses, and this has, in a few children, produced effects similar to irradiation. We have not done it more often because it does require lumbar puncture in the presence of increased intracranial pressure, but it is definitely possible to treat them this way.

We have done some microbiological assays of the spinal fluid on those children who have been on Methotrexate, and who have developed these symptoms. Dr. George Foley found no antifolic acid activity in their spinal fluids. After the intrathecal introduction of small amounts of Methotrexate there would be, a few days later, still a small amount of this activity in the spinal fluid. One patient responded to one administration of drug via lumbar puncture, and has never had another central nervous system symptom. We cannot explain his response.

The terminal episode in this child was different from the usual course of events in these children. As Dr. Byers pointed out, they usually recover from their central nervous system symptoms and get along very well. They may have a second episode, even a third, respond again, and do well again. The puzzling aspect of this child under discussion was that he did not respond to the second course of irradiation. We knew that something else must be amiss. We could not find bleeding, we could not find infection, but we could not rule out an intracranial neoplasm. I am afraid that if Dr. Farber were to ask for our clinical diagnosis before autopsy, we really did not know what was going on.

DR. FARBER.—You answered the question I was about to raise. Dr. Diamond, would you like to comment?

DR. LOUIS K. DIAMOND.—More than twenty-odd years ago, Dr. Jacob Furth, working on leukemia in mice, was able to isolate strains of leukemic cells which gave rise to various symptomatologies. In one instance, the strain of cells regularly invaded the meninges.[2] It may, eventually, be possible to differentiate tumor cells by their clinical behavior, as Dr. Furth did in the animals.

DR. FARBER.—That is a very interesting possibility. We are retreating more and more from the reliance upon the strict morphological classification and are hoping to be able to define these cells in terms of their metabolic activity, and response to the agents that we use against them.

Dr. Neuhauser, would you say a word?

DR. EDWARD B. D. NEUHAUSER.—When we first saw the skull film at the time of admission to the Tumor Therapy Service, it was perfectly normal. At the onset of cerebral symptoms, the sutures were separated up to 1 to 2 cm. He was then treated, and thereafter no further separations occurred and the skull plates even came together again as his pressure was relieved.

DR. HARRY SHWACHMAN.—I think we were all in a dilemma as to what the final event was—but we know, I think, from some experience that intracranial hemorrhage is a very common terminal event in children with leukemia. In this case, the peripheral blood, the bone marrow, and the platelet count (although the platelet count stated here was 4,000) made us feel that this was probably unlikely, although it could occur. Conditions such as brain abscess were dismissed because this child had been given chemotherapy.

I would like to say a word about the use of antibiotics in these children. Because of their low white counts, they develop infections very readily and

the general policy is to use antibiotics liberally. We think that this permits the antifolic agents or other agents to become effective, and we sometimes save the child from succumbing to a serious infection—thus permitting a long remission. Terminally, we discover agents, bacteria or fungi which are not responsive to the antibiotics that are used. In other words, we have eliminated the susceptible organisms and we are left with resistant strains of organisms or with new organisms that are not usually found in children. I think this is one of the important problems that we are facing, and it means that not only is it important to look for new agents in the treatment of leukemia but also in the treatment of bacterial and fungal infection.

DR. FARBER.—Thank you, Dr. Shwachman. I suggest that we go on with Dr. Craig's findings now. The final clinical diagnosis was leukemia in remission, and a central nervous system disorder, undiagnosed.

DR. CRAIG.—It was our opinion that this child was, by all pathologic criteria, still in complete remission from his leukemia. There were no areas of the body in which one, if given that particular area, could say that this child had now, or had in the past, a leukemic process, so that we considered him to be in complete remission. His spleen was not enlarged, although the liver was enlarged by about one third. It has been a common observation that many of the children who die, apparently in complete remission, still have enlarged livers without leukemic infiltration. His adrenals showed the evidence of cortisone activity. There was separation of the cranial sutures, but we found no evidence of leukemic infiltration in and around these sutures, as has been postulated by some people.

The bone marrow had a slight hypoplasia, with a large number of megakaryocytes. There was evidence of osteoporosis and erosion of the bone but the trabeculae were clothed with osteoblasts (Fig. 1). The bone appears to be in the stage of repair from the previously heavily infiltrated osteoporotic state. There were a few submetaphyseal fractures in the ends of the ribs which were also in a healing stage.

The brain was approximately 150 grams overweight. The gyri were somewhat flattened, the sulci narrow, and on cutting there was an hydrocephalus (Fig. 2). This extended throughout the ventricular system. The meninges were opaque and thick over most of the brain, especially marked at the base of the brain. There was a sizable area of softening in the region of the basal ganglion, which is regarded as a small remnant of an abscess or infarction (Fig. 3). There was a similar area in the pons, which undoubtedly gave rise to the symptoms that Dr. Byers suggested of transection of the brain stem. The meninges over the vertex of the brain were thickened and slightly fibrotic, with mononuclear cells scattered through them, but without leukemic elements. In areas near the base of the brain there was a frankly purulent exudate with a great deal of degeneration and necrosis of the cellular exudate (Fig. 4). There was also a thrombosis of one of the basilar vessels. There were masses of necrotic polymorphonuclear cells, lymphocytes, and plasma cells in the meninges, and I am surprised that no

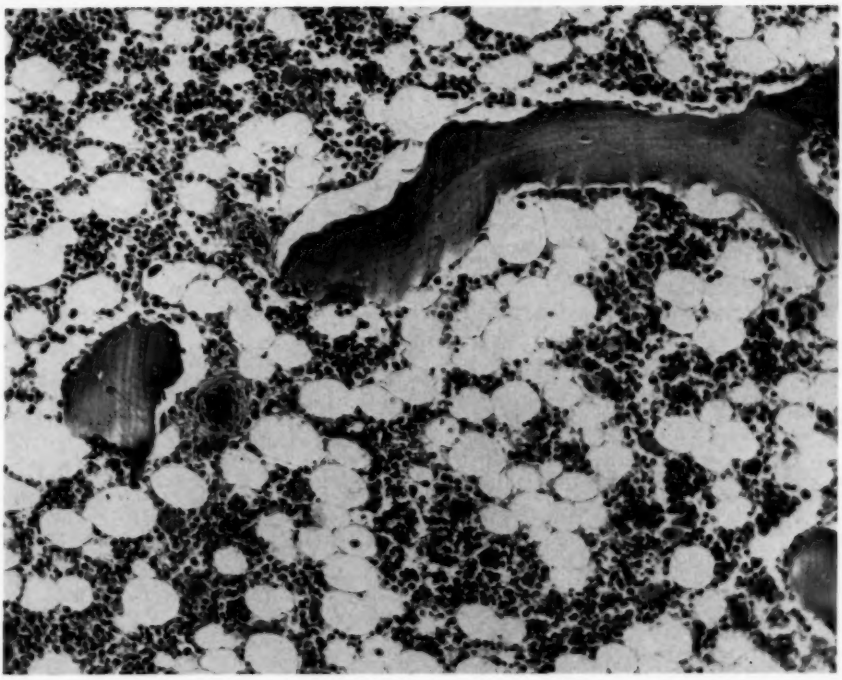

Fig. 1.—Photomicrograph of vertebral marrow. The marrow is mildly hypoplastic but no leukemic cells are present. The trabeculae are irregularly eroded, though partially recovered by osteoblasts. (Hematoxylin and eosin; ×165.)

Fig. 2.—Coronal section of the brain at the thalamic level. The ventricles are all dilated. An ischemic infarct is present on the left.

Fig. 3.

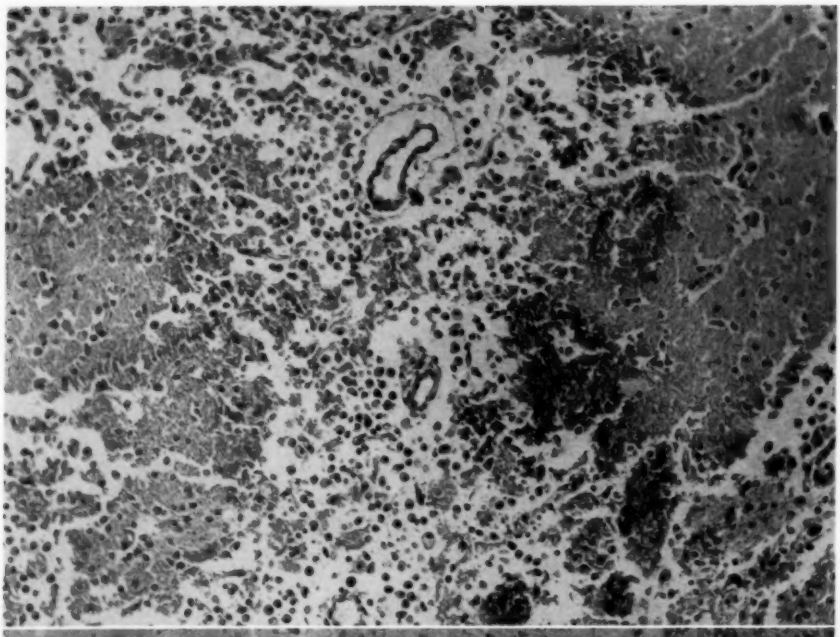

Fig. 4.

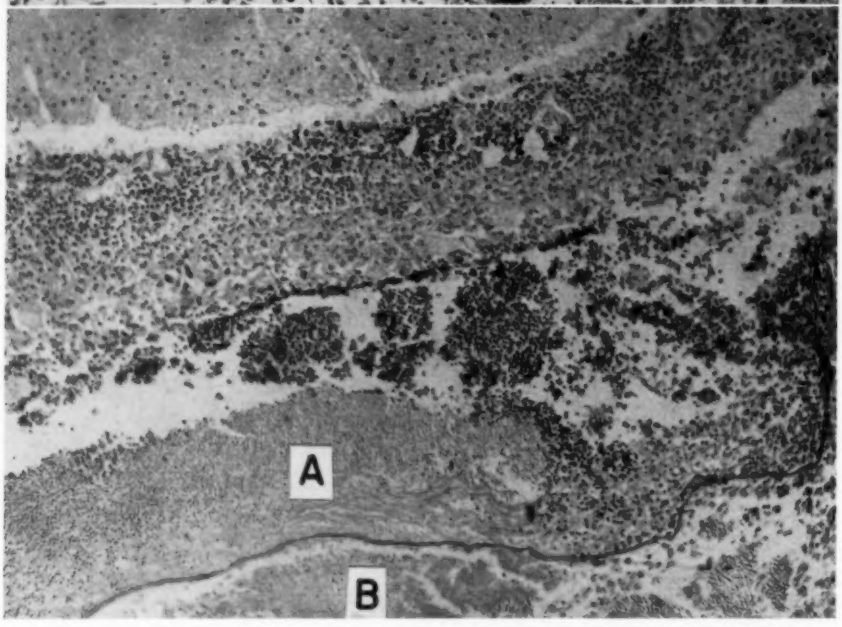

Fig. 3.—Photomicrograph of brain. The area of ischemic infarction and loss of brain substance contains many fatty macrophages. (Hematoxylin and eosin; ×110.)

Fig. 4.—Photomicrograph of brain. The meninges are heavily infiltrated with an exudate of intact and pyknotic polymorphonuclear leukocytes. The wall (*A*) of a meningeal vessel is necrotic, and the lumen (B) is obstructed by a thrombus. (Hematoxylin and eosin; ×100.)

more cells or polymorphonuclears were encountered in the lumbar puncture.

We believe that though leukemic infiltration may have been a part of the early picture, infection certainly played a large role in the terminal process. This involved the meninges and their vessels, with thrombosis and subsequent infarction of the brain. We were embarrassed by the riches of organisms in our postmortem culture from the brain, though the heart and lungs were sterile. From the brain we were able to culture *Aerobacter aerogenes, Enterococci,* and also a *Candida* organism. The latter we were not able to identify in the tissue sections. The reasons why the antemortem spinal fluid cultures were negative were probably the loculation of this meningitic process, and the antibiotic coverage.

We have not had to much of an opportunity to observe the disparity between the peripheral areas of the body and in the brain in regard to persistence of leukemic infiltration, although we have seen one other case in which clear-cut evidence of a pure leukemic infiltration in the brain was present, yet in all the other tissues in the body, no leukemic activity was found.

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Medical Progress

THE HISTORY OF INFANT WELFARE

BETHEL SOLOMONS, M.D., F.R.C.P.I., F.R.C.O.G., F.A.C.S. (HON.)

DUBLIN, IRELAND

I FELT highly honored when I received the invitation from the President and Council to deliver this lecture which was founded by Sir Wm. Fletcher Shaw in memory of his son. Meredith was educated at Oundle School where he worked hard and was a member of the Rugby XV. Although not medical, he took a marked interest in the College. When the war broke out, although he was married, he insisted on joining a fighting battalion. He was awarded the Military Cross for bravery. Later he was reported missing and, alas, he has never been heard of since.

Our late lamented President in his invitation said the lecture savoured of philosophy, and I fear I have never been a very wise philosopher, but I was most anxious to accept, chiefly because of my valued friendship with Fletcher Shaw, whom I call the Father of the College (or perhaps he might be called the twin father) and also because of the opinion, shared by all, of his professional and organizing abilities. "It is a man's own fault; it is from want of use if his mind grows torpid in old age." Thus spoke Samuel Johnson, and I trust there will not be too much torpidity in the remarks of the somewhat senior obstetrician who speaks to you today.

A philosopher is defined as a lover of wisdom, and I suppose with my name I should be wise, but I fear that many of my friends will agree that I am far from being placed in the same category as my ancestor, King Solomon. In our specialty we deal with many wives, but not, I hope, in the same way as the king. A philosopher, too, is defined as one who shows philosophic calmness in trying circumstances; that every obstetrician must do, and whether in dealing with the emergencies of practice, on behalf of either the woman or the infant, or even during the trying circumstances which may be encountered on the hunting field, one must be a philosopher. Having first decided that I am a poor one, perhaps I may claim to be included to a small degree.

The choice of a subject was a puzzle; several which I might have chosen have been ably done before. It was suggested that I might speak of what I might call my own hospital, the Rotunda, but that would have meant repeating to a large extent the works of Kirkpatrick and Jellett (1913) and O'Donel Browne (1947).

Ex-Master, Rotunda Hospital, Dublin.

The Meredith Fletcher-Shaw Lecture delivered at the Royal College of Obstetricians and Gynaecologists, Nov. 22, 1957.

As I have always been interested in babies, I decided on my present subject, for children are the most important people in the world, as Longfellow has so well said:

"Ah what would the world be to us
If the children were no more,
We should dread the desert behind us
Worse than the dark before."

It may be suggested this is not an appropriate subject for a College lecture, but I hold strongly that it is, and that the subject of infants should not be divorced from midwifery. In fact, the formation of the College was an important niche in the progress in the study of infants. I shall show later that my opinion is shared by authorities in other countries. During the past year, the College has demonstrated its feelings by conferring our Honorary Fellowship on the distinguished pediatrician, Professor Capon.

Before getting to the main thesis of my lecture, I want to say a few words about the medical student, especially in relation to his training from a humanitarian point of view; also I shall be considering at what period in his curriculum he should be trained in the study of infants.

All medical students should join a dramatic society. This would make them think; it would give them poise, train their memories, teach them how to speak and how few speakers try to enunciate. They would be reading plays which would give them an insight into life and thus give them a better understanding of their patients; in fact, they would have that psychological instinct, useful whether dealing with the adult or with the infant. I believe there should be lectures in psychology in the early years of the medical course in gynecology.

Life is a fluke, and whom the medical student will meet is due to chance. He may be lucky enough to encounter men and women who will wake him up. He may be encouraged to read, e.g., Thomas Browne, Walt Whitman, Edward Carpenter, and Osler's *Essays*, but if this encouragement is not given, the student may well become an over-the-counter doctor. Drugs and operations may be ordered when a good "pep" talk will be more helpful. The text for the medical student and the qualified doctor is: "Let me make my patient well, let me try to understand him mentally and physically, let me be gentle." What will the student do when he is qualified? Let him have a good look round and decide whether he wishes to do general practice or to specialize.

The Oxford Dictionary defines "infant" as a child under 7 years of age; this should be changed. I would give a limit of 1 year in the definition of infant.

HISTORICAL

The care of infants dates back for many centuries; it has been a pertinent problem and still is today. Probably the first mention of infant care is in regard to the rite of circumcision. This was advised as a religious rite, but I believe that this, like many other such religious laws mentioned in the Old Testament, was primarily ordained for reasons of health. In spite of the correspondence against this operation recently in the medical journals, I know it has every advantage and no disadvantage, if performed according to the rabbinical method.

There are numerous references to infant welfare in the Talmud, especially in the Ebers papyrus where

there is mention of the custom of rubbing the infant with salt and putting him in swaddling clothes. Various Chinese and Indian authors refer to infant care. Hippocrates, Celsus, Galen, and especially Soranus were strong advocates of breast feeding (Henderson, 1943).

Italy was the nation in the forefront, and in 787 Darteus founded an asylum for homeless children in Milan (McNeill, 1936). This was followed in 1340 and 1411 by clinics in Venice and Florence, but the dark ages for infants persisted until near the end of the seventeenth century despite the active interest of the churches.

In 1473 the first textbook in the vernacular was published in German by Metlinger and in 1518 an important handbook of pediatrics appeared in Venice, *De Morbis Puerporum* by Mercuriales. The only one written by an Englishman before the seventeenth century was by Phaers in 1545. Even our great Jonathan Swift in his "Modest Proposals" in 1729 treated with scorn the unhappy state of childhood as he found it in the adoption laws.

Until the latter part of the sixteenth century there was a strong feeling against the employment of male doctors at childbirth. Paré (1517-1590) was largely instrumental in removing the ban.

About this time, Chamberlen invented the obstetrical forceps, which was a real lifesaver of infants, even though it must have killed many through the action of meddlesome obstetricians.

That wonderful sixteenth century Saint, Vincent de Paul, was very early in the fight for infant welfare. According to Schlesinger, he created an orphanage and foundling hospital and the first organization for health visitors. His statue outside a children's hospital in Paris is a fitting tribute to his memory.

In 1676 L'Hôpital des Enfants Malades was opened in Paris for foundlings. Previous to 1740 the medical profession was apparently not very much interested in infant welfare, for obstetrics was in the hands of midwives and was an undeveloped science.

In 1741 Coram (Caulfield, 1930), a pioneer, opened the Foundling Hospital in London. He was painted by that great artist and philanthropist Hogarth, and Joshua Reynolds and other painters exhibited for the benefit of the hospital. This line might be followed by the artists of today.

Cadogan, who lived between 1711 and 1797, was in the forefront of early workers for infants; among other things he advised less clothing, for babies were nearly smothered in clothes, and he was a strong advocate of natural feeding. He became a Fellow of the Royal Society.

Propaganda was started by a play attributed to Hanway in 1762. It was called *The Bastard or the feast of the Church-wardens, a dramatic satire in two acts, as it is acted today within the Bills of Mortality.*

George Armstrong, in 1769, one of the early English pediatricians, described pyloric stenosis and founded a dispensary for the infant poor in 1769, while about the same time Rosne von Rosenstien in Sweden was named the father of pediatrics.

There was a pre-health Act in 1793, which provided that parents whose only resources were the results of their labors were given the right to the nation's succor.

About that time also, wet nurses were put under the care of a Recommanderesse in France and in each year five to six hundred people were jailed for not paying their wet nurses. What a pity it is that more people today are not jailed for forgetting to pay their medical attendants!

It appears that obstetricians first taught pediatries in 1787 in Denmark. Saxtorph designed a shield to prevent a baby being crushed while suckling. A famous man, he was succeeded by his son.

Apart from Phaer's book already mentioned, a not very illuminating book by Dewees appeared in 1825. An amusing treatment suggested by him was that in the care of inverted nipples a young puppy should be put to the breast at frequent intervals.

Hirschsprung (1830-1916) was the father of Danish pediatries. In 1840, Levy, who had been a pediatrician, became professor of obstetries in Copenhagen. Today the professor of obstetries is still professor of diseases of the newborn.

In 1844, Haartman, a professor of surgery and obstetries, wrote a book on diseases of children. He had a large experience for he was the father of 24 children.

In 1802, Napoleon founded a hospital for sick children. What a busy man he must have been with wars, wives, polities and child welfare!

In 1852, Great Ormond Street Children's Hospital was first opened, with ten beds and a small outpatient department. The history has been well told by Herbert Rutherford. An outstanding benefactor of the hospital was Sir James Barrie who gave to it the whole rights of *Peter Pan* in perpetuo.

France was advanced in its efforts to improve infant health, apart from other considerations because of its small birth rate. Marbeau, in 1844, started the first nursery where women could leave their cradles. Lay authors were not slow to help, and in the nineteenth century Dickens and Victor Hugo drew attention to the need for many improvements. Bowman published *Poems of Infancy*, related by Foote (1919).

In 1872, the Infant Life Protection Act was enacted with its important point that anyone taking charge of a child under 9 must inform the local authorities. Some of the handywomen, or gamps, were dangerous, and in 1881 the Midwives' Institute was founded.

This was followed in 1890 by the first Midwives' Bill, with State registration of midwives. Strange to say, this Bill was opposed by the medical profession, because it was thought it would interfere with their practice. In 1902, the Midwives' Act was passed and the Central Midwives Board created. It may be well said that the legislation about midwives enacted between the years 1881 and 1902 made these years a peak period for the welfare of infants.

In 1901, Gouttes de Lait, an organization to provide adequate diet was established in France.

One of the first politicians to help was John Burns, President of the Local Government Board of Great Britain in 1906, who said in the House of Commons that mothers should be taught to look after their children, have a good home, and be efficient housekeepers.

In the early part of 1900, various conferences were held, e.g., an Infant Welfare Conference in Paris in 1905, and a national conference on Infant

Mortality, under the patronage of Edward VII and Queen Alexandra in 1906. In 1906, Lady Aberdeen, the wife of the Lord Lieutenant of Ireland, instituted her splendid Infant and Child welfare schemes. These services were voluntary at first, but the Dublin Corporation took them over later with paid officials. In 1915, the very important Notification of Births Act became law.

Between 1914 and 1918 the number of Health Visitors in England rose from 600 to 2,577, and it may be remembered by some of the senior obstetricians that there was a jewel fund established about this time, when women sent in thousands of pounds worth of jewelry to be sold for the benefit of infant welfare. This stirred the imagination of the public, and in 1918 the Maternity and Child Welfare Act was passed. The increasing interest of the government in babies, is shown in the fact that the grant for Infant and Maternal Welfare in England in 1915 was £11,000, and in 1919 £218,000.

In 1934 the first training school for children's sick nurses was started in Sweden.

In 1947, in an important communication, Lewis and Blackwood suggested that infant deaths might have been prevented by (1) better prenatal care, (2) better obstetrical facilities and deliveries, (3) better routine care of the premature baby, (4) better medical treatment of the baby, (5) better social and economic conditions, (6) closer cooperation between hospital and public health staffs, (7) better mothercraft, and (8) better standard of health visiting and follow-up.

PRENUPTIAL INVESTIGATION

I believe that all future parents should be examined psychologically and physically with a view to the welfare of future progeny. Marriage guidance councils (or, as they may be called, prenuptial clinics), or, alternatively, a wise physician, should be consulted. It has been found that these clinics have not diminished the marriage rate in France. The presence of such diseases as tuberculosis, syphilis, and especially diabetes, should be determined. The blood should be investigated, especially the blood groups, to prevent an Rh-negative woman from marrying an Rh-positive man. I would go so far as to suggest that a rectovaginal examination and possibly a tube testing should be carried out for the woman, and a semen examination for the man, i.e., for those whose greatest desire in marriage is a healthy infant. In spite of this, two people in love will marry.

Haig Ferguson (1912) spoke of the ideal conditions for marriage to produce the best babies: (a) good physical health and mental balance, (b) a pleasing exterior, with beauty if possible, and (c) beauty of character. These, however, should be difficult to ascertain during a short prenuptial visit and, of course, society cannot be modeled on the pattern of a stud farm.

To achieve the best babies Robert Browning suggests:

> "A people is but the attempt of many
> To rise to the completer life of one
> And those who live as models for the mass
> Are singly of more value than they all."

PRENATAL CARE

Prenatal care is one of the most valuable assets in the saving of infant life and, although there were efforts in

other countries, Ballantyne (1861-1923) may be regarded as the father of this valuable lifesaving measure. When I took charge of the Rotunda in 1926, I found that Falkiner, who was then assistant master, had started a clinic about a year before. I organized a clinic on a firm basis.

The following should be the aims of a prenatal clinic, from the standpoint both of the mother and of the baby:

1. Supervision of health of expectant mother, both general and obstetrical. The consulting physician will look after her chest, etc., and the specialist will be on the watch for the toxemias, for threatened abortion, in fact for anything which may lead to fetal loss.

2. Education in health and care of the infant. I doubt if this is done to a great enough extent.

3. Provision of nourishment.

4. Psychological instruction. Are maternal feelings transmitted to the infant? From my experience I believe they are, and the attendant should use his influence to see that the pregnant woman is happy in body and mind. There is no scientific proof of this.

5. Relaxation, instruction about labor and any other point which will give more confidence to the patient. An intelligent physiotherapist will help.

6. Advice as to labor in the hospital. I believe if at all possible first babies should be born in the hospital or in a well-appointed nursing home. Too many have been lost through remaining in their own homes. This is a point under discussion today, and there is much correspondence in the medical journals. It must not be forgotten, too, that, whereas a first confinement may be without incident, the grand multipara may have complications.

7. Special care of illegitimate babies because of the enormously greater mortality in this class.

8. Early prenatal care. This should start after the first missed menstruation. Many patients come too late.

As stated, Ballantyne is the great name in connection with prenatal care, but in France, as early as the nineteenth century, there were preventive measures.

Much has been done by the establishment of the United Nations Children's Emergency Fund (U.N.C.E.F.) and the Child Health Section of the World Health Organization. Even if the United Nations can be criticized for some of its actions, it is working for children.

HOUSING

I now come to a most important problem which is bound up with fetal mortality, namely, housing. The *New Statesman* deserves great credit for opening up its columns for correspondence. In one letter Dr. Dodds of Harrow relates how a mother went to a welfare clinic to leave her 1-month-old baby from 9 A.M. to 5 P.M. because she could not find a landlady who would take her *and* the baby. She was only allowed to remain in the clinic because the matron was charitable and disobeyed regulations. In another similar case, the mother abandoned the baby in a church. Some problem families were visited. Twenty-four families lived in 24 caravans at 15/6 weekly ground rent. There was one tap and one lavatory between them all. One 1-month-old baby was never able to

leave the cot; there was no room on the floor. The sequence of events is obviously: no house, misery, infantile death. And we are supposed to be living in a civilized age of missile bombs and housing shortage.

Lately, doctors at infant clinics got a circular from the Medical Officer of Health of London, telling them not to write asking for houses unless applicants had some serious medical condition, for whom 100 houses are set aside annually. There are 165,000 families on a waiting list, and the London County Council expects to produce 2,000 dwellings in the next three years. In the Press it is stated that there is no real housing shortage! This will be difficult to explain to the caravan dwellers. A letter from a hospital almoner shows "the trail of misery and unhappiness and the breaking up of families life consequent on the housing shortage. Solve this shortage and the sum of human misery to which an official blind eye is turned will greatly lessen."

G. Pater (1957) writes from Hertford that the homeless of London are lucky in comparison with other cities. He speaks of a pregnant mother and her young children having to spend the night in a park, and he tells of an illegitimate child whose mother had nowhere to take it except a public lavatory. He mentions Holland where an experiment has been tried whereby homeless families are taken to live in special communities. The family life is maintained and there is some degree of privacy. I shall refer to this when dealing with the problem in Dublin.

CARE IN LABOR

Want of care and what may be called ignorant obstetrics stand out as prime factors as causes of infantile mortality. The highest mortality that befalls the human race occurs on the day of birth. There is no doubt that statistics about infant mortality have improved since the College was formed, but much remains to be done. To what may the deaths be attributed? Some of the principal causes are asphyxia, trauma during labor, congenital defects, prematurity, the toxemias, the hemorrhages, malpresentations, and disproportion.

The modern treatment of asphyxia neonatorum shows great improvement over the time when the Schultze method was in vogue. More research into the causes and prevention of prematurity is necessary. Congenital defects cannot always be avoided, but preventive measures can be taken for the following: (1) some doctors are now endeavoring to have female children infected with German measles to avoid the possibility of congenital defects at a future birth; (2) over-radiation during pregnancy should not and must not be carried out; however, mothers who read this should know that an x-ray film to ascertain the lie of the baby will do no harm.

There is less injury to infants in labor than ever before. Better education of the undergraduate and postgraduate student and the nearby perfection in technique of the lower segment operation have been undeniable factors in producing these improved results. The problems of the toxemias and accidental hemorrhage have not been solved, but the improvement in fetal mortality in case of placenta previa is wonderful. Better education has diminished the death rate from malpresentations, prolapsed cord, and disproportion.

IMMEDIATE CARE OF THE NEWBORN

New terms seem to be constantly springing up. The word "neonatal" has been used for years; used with death, it refers to death of the infant during or immediately after labor. The term "perinatal" is more modern; perinatal death implies death from 28 weeks of gestation to the end of the first week of life.

The Scandinavian countries were, and are, very much to the fore in promoting welfare. Norway has certain rules to be observed before a doctor is allowed to practice as a pediatrician. In order to be recognized, he must have completed six months' service in internal medicine, six months in a surgical department, six months in a department of epidemiology, and three years in a children's department. In Great Britain and Ireland a pediatrician should have a diploma in Child Health and preferably a Fellowship. For students in Sweden the course is four months, and pediatrics is regarded as a principal subject in the final examination.

In my inspection of the medical schools of Great Britain and Ireland for the General Medical Council, I found that different schools had different methods. I shall not delve into these minutely; my findings will be found in my reports to the Council when published. In some places the babies are put in charge of the pediatrician immediately; in others, the pediatrician attends him in consultation with the obstetrician.

With regard to the training of students, in the majority of schools pediatrics has become part of medicine, and the examination is in connection with the final examination in medicine. In a few, the examination is in connection with the final examination in midwifery.

I am convinced that the student, during his residential midwifery period, should be instructed in the care of infants up to 6 weeks of age; he will have to look after them when he goes into general practice. Whether the obstetrician or the pediatrician should give this instruction is a moot point. The candidate should certainly be asked questions about the baby at the final examination in midwifery. Diseases of older children can be dealt with in connection with medicine.

At the time of writing, the General Medical Council, is considering the curriculum. At present, the Draft Recommendations state under "Surgery" that instruction in medicine and surgery should include clinical clerkships in medicine, surgery and pediatrics for a period of not less than 15 months in the aggregate, and under "Midwifery and Gynaecology" there is a "suggestion" that among other items that instruction should include the care of the newborn infant. I hope this suggestion will be adhered to by examining bodies.

Who should care for the newborn infant? Has the pendulum swung too far away from the obstetrician to the pediatrician? In my youth we looked after our own babies; we did it well, and, personally, I did a large consultation practice in infants. My Chief, Tweedy, excelled in his clinical lectures, whether they were on the best method of bathing a baby or on feeding or on illnesses.

I ran what was then called a Baby Club voluntarily for about ten years. To this, mothers brought their babies

to be weighed and to get general advice; the enterprise inspired a spirit of competition to turn out the best baby, and the mortality in connection with the Clinic was practically nil. Later, these Clubs were taken over by the Corporation with paid officials. I used to call my clinic a "school for mothers."

There must be cooperation between the obstetrician and the pediatrician, and I believe the Rotunda has solved the problem to a large extent.

Is the pediatrician too scientific in his outlook? In the old days we used to feed our breast-fed babies regularly by the clock; now there is a tendency to give it food whenever it cries. Regularity in feeding is as necessary for babies as it is for adults. Nowadays, too, when bottle-fed, he seems to be allowed to take as much as he likes; overfilling of the stomach must be deleterious.

Again, we used to be proud of our results in the treatment of premature infants. Warmth, fluids by the mouth or rectum, even a few drops of dilute whiskey, all helped our babies, combined, of course, with the more than necessary efficient nursing. Today starvation for a day or two seems to be the vogue, and I am convinced that I have seen babies die who might have survived if they had been given some nourishment. I suppose the pediatricians have statistics to support their view or they would not give this advice. Nevertheless, I would like to see a check investigation made on, say, 200 babies 3 pounds in weight, 100 to be treated in the old way, and 100 in the new.

PREVENTIVE HEALTH ORGANIZATIONS

Organizations for the preservation of health of mothers and babies are now established all over the world. Jundell (1944) gave a masterly account of the pediatric clinics of the universities and colleges, as well as the research institutions, in Sweden, and McCleary (1935) mentioned the formation of the Infant Protection Society following the execution of Margaret Waters for baby farming.

In 1892 Consultations des Nourrissons were opened by Budin in France. Lady Aberdeen's pioneer work in Ireland has been mentioned. In 1954 in Finland, there were 3,675 child welfare centers. In Northern Ireland in 1955 there were 183 child health centers.

The literature in regard to the formation of societies for infant protection was profuse in the early part of 1950. One of the most important early centers for child psychiatry was opened in Norway about 1954. In Britain, the number of health visitors, who have been shown to be instrumental in the saving of infant life, rose to 2,511 in 1918. In Malaya, where conditions were not good, Haridas (1947) gave figures about Singapore. He emphasized that institutions for child welfare there diminished mortality and suggested improvements.

There is no need today to dwell on the necessity for preventive health organizations, but they must be kept up to standard and their activities and results examined at frequent intervals, so that the authorities and doctors will not get too smug. At these clinics pressure should be brought to bear on parents to have their babies inoculated according to modern methods. In Finland 85 per cent of infants get B.C.G. vaccination. Dr. Cowell (1955) of the National B.C.G. Committee for Ireland has supplied me with figures

showing a gradual increase in the percentage of 0 to 5 age groups vaccinated. From 1949 to 1955 the total number vaccinated was 65,136, or 18 per cent of the available population in these groups.

ADOPTION

Formerly, baby farming was a menace, and many infants were murdered. The adoption laws and the Notification of Births Act put a stop to this. It was not until 1927 that legal provision was made for adoption in Great Britain; this saved the lives of babies and gave pleasure to many childless parents. With regard to the latter, there is an interesting psychological sequel. In perhaps a month or two the new parents have forgotten that the child is not their own, and, even later, if the mother is lucky enough to bear a child, and this sometimes happens, the adopted one still receives complete parental affection. In Ireland the law was lately altered so that the adopted child legally takes the name of his or her new father, and this prevents the stigma of illegitimacy in later life. Homes have been provided for unwanted babies who would otherwise have helped to swell the mortality rate. Since the Act came into operation, there have been 4,517 adoption orders.

ILLEGITIMACY

This subject requires much investigation. Although the unmarried mother is in a better position today than she was in the past, the lot of her offspring is precarious. It seems a far cry from the time in 1473 when a girl became pregnant or overlaid her baby so that she could get a job as a wet nurse. Cheltenham got a bad name for the mortality of illegitimate babies but in a letter (1957) Dr. Bramley, the County Medical Officer of Health, says that in the past three years the number of deaths of illegitimate children under the age of 1 year has not been a marked feature. I suggest that inquiries should be made as to the method in which this diminution has been brought about. Bramley states that in better-class residential boroughs in England there is a high illegitimacy rate.

In the *Economist* of Aug. 17, 1957, there is a table showing the percentage of illegitimates among all live births: Austria 15.5, Sweden 9.8, Germany 7.7, France 6.7, Denmark 6.1, United Kingdom 4.6, United States 4.4, Canada 3.7, Norway 3.5, Belgium 3.2, South Africa (European) 1.6, and The Netherlands 1.4.

In England and Wales the number of illegitimate infants born in 1932 was 27,011, and in 1955 it was 30,918. The death rate was 32 per thousand. In Eire in 1955 the mortality of illegitimate babies was 71.31 per thousand, and of legitimate ones 37; the total was 1,230.

I do not intend to weary you with more figures in relation to the death rate for illegitimate babies. It is the same dreadful tale everywhere. These babies have as much right to live as their legalized brothers and sisters, and it is up to the medical profession to find some means for improvement. Efforts are being made; homes are provided for the unmarried mother where she can live with her baby, but, as can be readily understood, the bastard on the average does not get the care and affection bestowed on the legally begotten child. Not only the doctors must try to improve matters; almoners must renew their efforts; infant welfare organizations must do the same and the nursing profession cooperate

TABLE I

COUNTRIES	STILLBIRTH RATE PER 1,000 LIVE BIRTHS		PERINATAL MORTALITY RATE PER 1,000 LIVE BIRTHS		NEONATAL MORTALITY PER 1,000 LIVE BIRTHS		INFANT MORTALITY RATE PER 1,000 LIVE BIRTHS		INFANT MORTALITY, 1954
	1926-1930	1946-1950	1926-1930	1946-1950	1926-1930	1946-1950	1926-1930	1946-1950	
Austria	30.0	21.5	x	47.8(*a*)	50.8(*b*)	39.3	117.2	75.6	50
Belgium	27.5	25.7	x	48.6(*c*)	35.3	30.9	101.2	62.8	x
Denmark	23.9	18.2	46.4	34.7	32.3	20.5	82.3	37.7	27
Finland	27.2	18.7	48.6	35.1	35.5	23.9	87.9	51.9	34
France	29.7	20.9	x	x	35.4	28.4	94.3	62.0	38
Germany xx	32.4	22.5	x	50.3(*d*)	43.2	37.4	94.0	70.7	46
Ireland (Republic of)	x	37.5*	x	53.7*	26.2	25.9	70.3	56.7	39
Italy	37.8	32.5	55.3	52.6	38.7	33.8	119.4	76.5	59
Netherlands	25.7	20.0	42.8	34.2	24.0	18.1	56.4	30.9	22
Norway	25.4	17.8	x	30.5	24.5	16.0	49.5	31.9	x
Portugal	41.9	43.7	x	x	48.5(*e*)	34.4	145.1(*f*)	107.1	96
Spain	23.8	26.4	x	x	x	24.3	130.7	76.5	54
Sweden	26.8	20.9	45.0	35.2	26.4	16.8	57.6	24.0	19
Switzerland	25.0	16.7	47.6(*g*)	37.5(*h*)	28.9	24.3	54.0	36.0	30
United Kingdom (England and Wales)	42.0(*i*)	24.6	63.9(*i*)	40.8	31.8	21.1	67.9	36.3	27
Scotland	x	30.8	x	50.5	36.5	26.1	85.4	47.3	31

x—Not available.
xx—German Federal Republic for 1946-1950.
xxx—Stillbirths and first week deaths.
*—Estimated 1954.

(*a*) Average of 1949-1951.
(*b*) Average of 1926-1929.
(*c*) Average of 1948-1949.
(*d*) Average of 1949-1950.
(*e*) Average of 1929-1930.
(*f*) Average of 1926, 1927, 1929, 1930.
(*g*) Stillbirths and deaths under 9 days of age.
(*h*) Average of 1946-1949.
(*i*) Average of 1928-1930.

(From Deeny, James A.: Perinatal Mortality in Ireland, Irish J. M. Sc., August, 1955, p. 350.)

in the determination that in the future the mortality of the illegitimate child will be no higher than that of the legitimate.

INFANT MORTALITY

With the vast improvement in child health services, prenatal clinics, and obstetrical technique generally, infant mortality has diminished through the years. The most disturbing features are prematurity and illegitimacy. I shall not give the hosts of figures which I have obtained. Renault and Labeaume in 1937, spoke of the enormous number of abandoned babies, but now the number is infinitesimal, and this cause of mortality can be overlooked. In 1912 in France there were 124,000 abandoned babies. Although I am devoting a section to a consideration of Irish statistics, I shall include Deeny's mortality table here (Table I).

It will be seen from this table that the infant mortality rate in 1954 varies from 19 per thousand in Sweden to 96 in Portugal. Italy is next highest with 59, and Spain follows with 54. The stillbirth rate for 1954-1950 varies from 16.7 in Sweden to 43.7 in Portugal, and the perinatal mortality from 30.5 in Norway to 53.7 in Eire. For the neonatal mortality over the same period, Sweden again comes first with 16.8, and Austria last with 39.3. It is difficult to account for these divergent figures; possibly, grand multiparity in such countries as Portugal, Spain, and Eire might be etiological factors. The statistics on New York City which I have received from Dr. Greenstein, the senior statistician, are excellent. In the period 1950 to 1956, the perinatal mortality rate varied from 29.5 per thousand in 1956 to 31 in 1950, while the neonatal death rate over the same 7 years is also consistent. The lowest was 17.9 in 1954, the highest 19.1 in 1950. Last year it was 18.6 per thousand live births.

I have lately visited Portugal and, as the rate there is the highest in Europe, I tried to find out the reasons. The mortality per thousand under 1 year in the period 1915-1919 was 167.23, and in 1955 it was 90.24. The following causes were given: overpopulation, want of education for mothers, poverty, bad housing, starvation, syphilis, prematurity, and illegitimacy. It was suggested that if the Azores islands were not included, as the people there were excessively backward and poor, the Portuguese figures might be better, but it is obvious that this country must try to improve, possibly taking a line from Sweden with its splendid figures.

In London the death rate for infants under 1 year diminished in 1955 to 23. In Northern Ireland the rate diminished from 39 in 1952 to 29 in 1956; the neonatal rate was 23 in 1952, and 21 in 1956. Every country is working for its children, but the figures are curiously varying and an investigation into this anomaly might yield results.

The Eire Minister of Health in a recent speech stated that in 1946 the infant mortality rate was 65 per thousand births. Last year it was 36. These figures do not allow us to be complacent.

EIRE

When I started my preparation of this lecture, I was not aware of all the efforts that had been made in our comparatively new country for infant welfare, and when I was furnished with

information through the courtesy of Dr. O'Regan and Mr. Whelan, and the officials of the Health Department as well as by Dr. Collis (1957), whose book on *Neonatal Paediatrics* is on the press, and from which he furnished me with extracts, I decided that a section devoted to Eire might prove to be a useful addition to the history of infant welfare.

During my Mastership in 1930, I instituted in a very small way what I think was the first department for sick infants in any maternity hospital. This consisted of a nursery of 7 cots looked after by untrained nursery nurses. We had no funds then, but, when I managed to persuade the Governors to partake in the Sweep Funds, better conditions were possible and a unit was set up under the inspiring direction of Dr. Collis, with Dr. McClancy as Deputy. The head nurse, Sister Moran, is able to keep nearly any baby alive. The Dublin Corporation paid for the infants; now they come under the Health Act. The treatment of babies is not confined to those born in the Rotunda Hospital: the same applied to the excellent departments in the National Maternity and Coombe Hospitals; cases from outside can be admitted to the Paediatric Unit.

Postgraduate teaching is provided for in all the children's hospitals, as well as in the maternity hospitals. Lectures are given to undergraduates in the medical schools, and about 40 or 50 are given during the year at the Rotunda. The unit there consists of (1) 25 cots serving the needs of the labor wards and theater; (2) a special neonatal unit for babies born on the district and referred by outside doctors for such neonatal conditions as hemolytic diseases. This consists of between 30 and 35 cots, each a single, small, self-contained ward, a breast-milk bank, a milk kitchen, and an operating theater designed for neonatal surgery. The treatment of infants cannot be separated from obstetrics and yet it must needs take the child beyond the care of the obstetrician, because such abnormalities as hemolytic diseases, subdural hemorrhage and infections are more for the pediatric specialist. In addition, the Rotunda has a special outpatient department welfare center for the infants on its service. Here healthy babies are brought for weighing and advice. This is really a continuation of the baby club idea. Also, the sister-in-charge has many of the babies visited by her specially trained nurses. Apart from other advantages, it is a good training for postgraduates and students. At the end of six weeks they are sent back to their family doctors and the city welfare clinics, or both. Staff arrangements now include: (1) a Director and a Deputy Director both of consulting rank, (2) a resident pediatrician of registrar status having previous pediatric experience, (3) a resident obstetrician who is seconded from the junior obstetric staff; (4) postgraduate students. Teaching plays an important role. Dr. Collis includes two pediatric questions in the final examination in obstetrics. He says, and I cordially agree, that this is a better plan than having a separate paper, as the newborn baby and his mother must be considered together by the family doctor. Once more I reiterate, the management of the newborn infant must not be divorced from obstetrics. The pediatric staff members now examine all the newborn babies immediately after birth, take charge of the abnormal cases, and do a daily round of the

puerperal wards. They do not take the responsibility away from the obstetrical staff and their students for the first ten days of life, but rather work beside them. This coordination of pediatrics and obstetrics has been very satisfactory, but one has only to remember the subject of stillbirth with all its complications for the obstetrician, the general practitioner, the pediatrician, and especially for the family, to recognize how much there is to be done in the future.

I am grateful to Dr. Collis for all the information he has given me. Perhaps I have given too much detail about the Rotunda, but I have done so because I feel that its setup is an example for any maternity hospital to follow.

Coming now to Eire in general, with regard to perinatal mortality, Deeny in his table shows that a death rate of 53.7 per thousand in the period 1946-1950, appears to be the highest, with Norway (30.5) the lowest, but the figures of some countries were not available.

In speaking of infant mortality in Eire, it must be remembered that we have the oldest marriage age in Europe, and the highest fertility rate per marriage. In his excellent paper, Deeny quotes Feeney (1953) from the Coombe Hospital, giving the causes of 477 stillbirths. It is stated that the loss of life from perinatal mortality comes close to the cancer rate.

Dugald Baird (1955) has produced evidence that there is a correlation between prematurity and pregnancy at short intervals, and also between prematurity and hard physical work during the last three months of pregnancy. The former would apply to Eire. Perinatal mortality has become so significant that arrangements have been made with World Health Organizations for a study on lines agreed between Eire, Sweden, and Holland.

What other steps are being taken in Eire? In the Report of the Department of Health for 1954-55, it is proposed by the end of 1955 to have an additional 1,500 beds for infants. There have been various acts promulgated by the Government, and details of these will be found in the Reports from the first one in 1945 to the latest.

In 1934 compulsory inspection of private maternity homes became law, a necessary measure. Details of the grants and the staffs employed by the Government and the Corporation will be found in the various blue books.

Immunization.—There are 16 clinics weekly, held by Corporation officials, for diptheria and pertussis, and now tetanus is included. Difficulty is experienced in getting mothers of the lower income groups to allow their babies to be immunized. Propaganda work is necessary. B.C.G. is largely given and there is a national committee in connection with St. Ultan's infant hospital.

Generally speaking, midwives look after the babies during the first week, and then district nurses combine general nursing with infant welfare. Prenatally the nurse sees the patient not later than the sixteenth week, and then gives three more visits; this is not soon enough and there are not enough visits, even though there is a provision for more attendance if necessary.

Choice of Doctor.—Under the Corporation Health Act of 1953 we read: Just as the woman has a choice of

doctor, so the doctor has a choice of patient, and he has the right, if he wishes, to refuse to accept any woman under the scheme, but he cannot refuse her under the scheme and accept her as a private patient. I have been told of patients, not in Eire, where an urgent operation was required and the information was given that there were no free beds available, but private beds could be managed. This is nearly blackmail. In Dublin the doctor must attend at least once after delivery, and for this, the few prenatal visits, and attendance at the actual confinement, he gets £7.7.0. The number of visits and the payment might be increased. The fee of £3.3.0. for the consultant whom he may have to call on a difficult case is too small.

Housing.—As in other countries, there is a housing shortage in Eire and many families still live under slum conditions. Efforts are being made to correct this, for it definitely leads to infantile death and disease. In the Department of Health Report 1953-1955, it is stated that the number of new dwellings erected and reconstructed in 1952-1953 was 15,733 and in 1954-1955 it was 14,782; but Eire is low in housing progress, ranking seventeenth among European nations, according to the United Nations Commission for Europe. The latest figures given by the Commission show that, per thousand inhabitants, West Germany has put up 11, Russia 8.2, Sweden and Switzerland 7.9 each, Finland 7.5, Greece 6.9, Holland 6.4, Britain and Austria 6 each, France 5.5, Belgium, Czechoslovakia and Italy 4.8 each, Denmark 4.5, Spain 4.2, Ireland 3.8, Poland 3.3, Roumania 3.1, Yugoslavia 2.1, East Germany 1.8, Hungary 1.6. In the last report from Dublin it is stated that during the past 9 years, 25 million pounds have been spent on providing 15,000 dwellings and, in addition, 9 million have been advanced for loans on 6,000 houses—not a bad achievement.

ISRAEL

As I have devoted some space to the comparatively new state of Eire, I decided to give even a smaller space to the newer state of Israel, which I visited a few years ago. I was impressed by the splendid work done by the Government, and very largely by charitable institutions. In making these notes I have been helped by literature supplied to me by the Minister of Health. A suitable quotation for Israel is from Jeremiah: "I will bring them from the north country and gather from the coasts of the earth and with them the blind and the lame, the woman with child and her that travaileth with child together."

Before 1948 when the state of Israel was established, the infant mortality rate was high and there were no organized health departments. In 1948 a Ministry of Health was established. In 1955 there were 370 maternity and child health stations; in these 31,185, i.e., 80 per cent of all infants, were under supervision. It was hoped then to provide inoculation centers. The infant mortality rate in 1955 by religion was: Jews 34.5, Moslems 62.7, Christians 56.1, Druzes 59.5 per thousand. The whole mortality per thousand between 1950 and 1954 was: in 1950, 45.6, and in 1954, 34.5. My listeners will derive profit from reading the Israel literature about the

health services. The infant morbidity rate is high because of gastroenteritis and respiratory diseases.

SUMMARY AND CONCLUSIONS

1. Though some may consider it is outside the scope of this Lecture, I suggest there should be improvement in the training of medical students in such academic subjects as the history of medicine, as well as training in psychiatry early in his course.

2. The welfare of infants has been a subject of interest from Biblical days up to the present. Propaganda urging its importance is found in the books of lay authors. Kings and Queens of England have shown interest in the health of their infant subjects.

3. Prenuptial investigation, especially in relation to the Rh factor, should be made and prenatal and intranatal care must be sustained. Much research is necessary to prevent prematurity, and the care of illegitimate babies must be tightened.

4. Housing everywhere must be improved.

5. Should the pediatrician or the obstetrician care for the newborn infant? My answer is: there should be close cooperation between them and the student should get instruction during his term of residence.

6. More preventive health organizations are necessary.

7. The technique for dealing with the newborn infant at the Rotunda Hospital is described.

Apart from those I have mentioned, I have received courtesy and literature from the Health Departments of Eire, the London County Council, the French Embassy in Dublin, the Librarians of the Royal Society of Medicine, and the Royal College of Physicians of Ireland, Professor Brandstrup of Copenhagen, Sir Ernest Finch, Miles Phillips, and others.

Many poets have sung about infants. Blake in "Songs of Innocence":

> "And can he who smiles on all
> Hear the wren with sorrows small
> Hear the small birds' grief and care
> Hear the woes that infants bear. . . ."

I shall conclude with some lines from our own W. B. Yeats to his child:

> "The angels are stooping
> Above your bed
> They weary of trooping
> With the whimpering dead.
> I sigh that kiss you
> For I must own
> That I shall miss you
> When you have grown."

ADDENDUM

I want to draw the attention of those interested in the history of infant welfare to a very vital book, *Children of Europe*, by Dorothy McArdle (1951). In this she shows what the Nazis have done to children; millions were slaughtered, thousands of others suffered lasting injury from disease and trauma. It is impossible to estimate the amount of harm done; the problem of modern delinquency is a direct result in some countries. McArdle refers to the number saved by welfare centers and even by Flemish nuns. I have not the space to give a description of the torture and death of children in every country occupied by the enemy. There is a mass of important material in this book which should be studied by all interested in the future of infants.

As an epilogue to this lecture it is pleasant to report the gift of that great philanthropist, Lord Nuffield, for the endowment of a Professorship of Child Surgery at the Institute of Child Welfare and the Great Ormond Street Hospital.

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Comments on Current Literature

NECROTIC ARACHNIDISM

Cases of arachnidism reported in the United States are usually attributable to the black widow spider, *Latrodectus mactans,* and current handbooks for the identification of arthropods having medical importance list the black widow as the only spider in the United States the bite of which is injurious enough to require medical attention. A recent summary[1] of an extensive taxonomic and ecologic study, soon to be published, lists three species of *Latrodectus* in the United States and Southern Canada: *L. mactans,* distributed throughout Maryland, Indiana, and the midwest to Wyoming, Utah and Central California; *L. curacaviensis,* "the common black widow spider of New England, most northern states and probably southern Canada"; and *L. geometricus,* which is not common in this country, but occasional specimens of which have been found in Florida.

While authentic cases of arachnidism other than latrodectism have been described rarely in American medical literature, physicians practicing in some rural areas have realized for a number of years that spiders of other genera may inflict bites serious enough to require medical treatment, in some instances being accompanied by toxic systemic manifestations. In this connection two publications within the past year are of special interest, a preliminary report in *Science* for July 12, 1957, and a full report appearing in the *American Journal of Tropical Medicine and Hygiene* for March, 1958. These reports by Atkins, Wingo, Sodeman, and Flynn[2] are concerned with necrotic arachnidism resulting from the bite of the brown spider, *Loxosceles reclusus,* which is similar to the so-called "gangrenous spot" (brown) spider of Chile, *Loxosceles laeta.*[3] The senior author, in practice in rural and urban Missouri over a period of years, had treated a number of patients for the effects of a "brown spider" bite. In all instances the spider escaped, or was crushed beyond identification. However, the spider was always described as brown, and not shiny; absence of the familiar symptomatology of latrodectism seemed to preclude incrimination of the black widow. Symptoms recorded in these earlier cases varied, presumably according to the amount of venom received. Usually a thick wheal formed rapidly with almost immediate evidence of tissue necrosis at the site of punctures by the chelicerae. The necrotic area soon turned violaceous, then black and dry. Within a week's time the area sloughed out, leaving a deep, sharply-defined granular area surrounded by the raised edges of healthy tissue. The sloughed area, frequently quite large, usually persisted for several weeks with slow healing from below. In a few instances systemic disturbances of a general nature were recorded, including the occurrence of a rash resembling that of scarlet fever.

Within the past three years these authors have encountered in Central Missouri five patients in whom a similar clinical picture, considered compatible with necrotic arachnidism, followed the bite of a brown spider. In one instance the patient had a close-range view of the spider before it escaped, and was prompted to search

the premises for spiders resembling it for purposes of identification. A single female of *Loxosceles reclusus* was the result; some time later additional specimens of this same species were found along the cellar stairs in the same house. In a second instance, the patient was bitten lightly, and experienced no pain until the wheal had developed and he began to suffer generalized discomfort, apparently a systemic reaction. A survey of the premises revealed that the outbuildings were infested heavily by *L. reclusus*, with a large population in the entrance and along the steps of a storm-type fruit cellar visited daily by members of the household. The authors give one case history in detail as a striking example of the clinical picture, and include a series of photographs illustrating the skin rash and the progressive changes in the necrotic eschar.

T. W., a white woman, aged 33 years, was awakened at night by a sharp stinging sensation in the left deltoid area; lighting the bedside lamp, she noted a brown spider on the adjacent wall, but at the time did not connect her symptoms with the spider. Almost immediately a large reddened area developed in the deltoid region; itching was not a prominent feature. The pain increased in intensity with radiation down the arm on movement, or when the area was touched. Systemic manifestations, which became apparent within a few hours, included headache and marked restlessness. When the patient was examined nearly twelve hours following the bite, the blood pressure (right brachial artery) was 126/82, oral temperature was 99.6° F., pulse 96 per minute, respirations 22 per minute. In the left deltoid region there was a whitish, edematous central area about 1.5 cm. in diameter surrounded by a wide irregular zone of inflammation. The entire area was exquisitely tender with lancinating pain on the slightest pressure. Within another twenty-four hours, extensive extravasation of blood had occurred into the inflammatory zone surrounding the white central area. A generalized scarlatiniform eruption appeared over the entire body including the extremities. The rash reached a peak in three days and faded gradually with desquamation beginning on the second day. In this patient the blood count and hemoglobin level were not remarkable; urinalysis showed a trace of albumin. During the next few days, the central area of the bite became necrotic, turned black and finally sequestrated. By the end of one week, there was a deep ulceration extending down to the musele; tenderness disappeared very gradually; healing and scar formation required about ten weeks. Therapy in general was supportive; however, in this particular patient prednisone was started on the first day, 15 mg. three times daily, because of the severe systemic reaction. It was continued for one week at this dosage, being reduced gradually over the second week, and discontinued entirely after fourteen days. No particular effect of the prednisone was noted. In two of the five patients fever was a more marked feature of the response, and in one patient the white count reached 25,000. Protein in the urine in some degree was common, but no gross hemoglobinuria occurred. The characteristic eschar formation distinguishes the bite of this brown spider from that of the black widow in which necrosis is rare except as a result of strenuous local treatment, the use of tourniquets, or suction, etc.

The striking similarity of these cases of necrotic spider bite to the "gangrenous spot," cutaneous arachnidism of Chile[3] prompted the authors to undertake experimental investigations with laboratory animals. *Loxosceles reclusus*, males and females, in various stages of growth were kept in the laboratory for approximately one year. Food consisted mainly of the nymphs of the house cricket. Both male and female spiders were allowed to bite rabbits and guinea pigs. Some of the spiders "bit and detached very quickly; others remained with the fangs

sunk into the skin for from five to ten seconds, and in some extreme cases held the skin until forcibly detached. Almost without exception, the amount of venom injected, as evidenced by the effect on the laboratory animal, was proportional to the length of time the fangs remained in the skin."[2] Both rabbits and guinea pigs died following severe or multiple bites; one adult rabbit weighing about 8 pounds died violently within thirteen hours after having been bitten three times by a large adult female *L. reclusus*. Postmortem examination of this rabbit revealed the skin in bitten areas greatly thickened by hemorrhage and edema, gross subcutaneous hemorrhages and edema over a wide area, petechial and ecchymotic hemorrhages in skeletal muscles, in the serosa of the stomach, small intestine, and thymus, and shallow erosions up to 3 mm. in diameter in the gastric mucosa. Intussusception was present in this animal in the anterior portion of the jejunum and the distal end of the colon. In animals which recovered, the objective manifestations were comparable to those in human subjects: evidence of pain, hyperactivity bordering on convulsions, diarrhea, and in the case of one guinea pig which eventually succumbed, gross hematuria. Eschar formation was similar to that observed in patients. Several animals were sacrificed at varying intervals following the bite for a study of eschar formation and of the general systemic effects. Both male and female spiders are venomous and apparently bite with like intensity. Venom can be extracted from poison glands macerated in saline, and can be administered by injection. Since the South American workers had reported that rabbits recovered from several bites seemed to be immune to the toxin, and that mice could be protected from the venom by their serum, Atkins and his associates attempted the immunization of rabbits by bite, and (or) by injection. In two instances rabbits were protected against lethal doses after being bitten four times or receiving small repeated injections of venom. One rabbit, so treated, tolerated a large dose of venom intravenously in contrast to a control animal of comparable age and weight which died violently within 21 hours following a similar intravenous dose. The authors attach considerable significance to this preliminary observation concerned with the possible immune status of these animals.

The brown spider, *Loxosceles reclusus*, and a closely related species, *marylandicus*, is reported to be well-distributed in the midwest to western areas of the United States, and as far south as Texas.[4] The family of arachnids (Loxoscelidae) to which these species belong includes the spiders commonly known among naturalists as the false-hackled band spinners. While there is some individual variation in color, from dark brown to light brown, or yellow brown, in all specimens the cephalothorax bears a median area of darker color extending back from the eyes, which has been described as "pear-shaped" or "violin-shaped." The legs proximally are the same color as the body, but darken distally. The general body appearance is not that of shiny chitin like the black widow, but gives the impression of being somewhat roughened, or fuzzy (hackled). Full-grown specimens are of medium size, with females slightly larger than the males. Two enlarged photographs are included by the authors which show the characteristic markings in detail. While some species of *Loxosceles* can be seen out of doors, under stones, leaves, fallen logs, etc., *reclusus* seems to favor an indoor habitat, in or near human dwellings, spinning irregular webs in outbuildings, under steps, in storage closets, attics, in the folds of clothing hanging undisturbed.

In summary, the authors stress the similarity of this type of necrotic arachnidism to the "gangrenous spot" cutaneous arachnidism seen in some South American countries which is caused by the bite of *Loxosceles laeta*, and the fact that the clinical picture

in their cases of necrotic arachnidism resulting from the bite of *Loxosceles reclusus* is quite distinct from that associated with the bite of the black widow spider.

RUSSELL J. BLATTNER.

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Correspondence

[Editor's note: While it had been decided to close the discussion on pediatric practice with the June issue, the following communication from one who had previously contributed to the discussion is of so much interest that it was decided to publish it. Dr. Hammond's picture of pediatrics in a general practice adds an interesting point to the discussion.]

To the Editor:

Pediatrics in Practice

The statement that "your happiness is where you find it" has its implications for us in medicine. No doubt most of those who carry the gold-headed cane find tranquillity in the practice of our profession. There are many engaged in various branches of medicine who do not, and there is even documented evidence that some find no peace of mind in their practice of pediatrics.[1, 2]

There has been much discussion, some of it aired in "Letters to the Editor," as to why physicians have become disenchanted when they leave Hippocrates' ivy halls.[3–5] In some such cases the proposed answers boil down to the proposition that there is a dichotomy within our ranks—charges that those in the ivory towers of academic medicine do not prepare their students for worldly practice. The inference would be that our teachers do not know the medical facts of life so far as the general practice of pediatrics is concerned. Many of us doubt that such an explanation is entirely true, or, if it is true, that the answer is entirely as simple as this. Probably few academicians would prophesy more than one patient with Hirschprung's disease per generation among the flotsam and jetsam of their protégés' future general practices.

With such thoughts as these in mind, I studied the character of my own general practice during a year. It was no surprise when I came through with some findings which most physicians in general practice would have surmised even without the efforts of such scientific abracadabra. The truth may sting, but the figures revealed that the vast majority of the pediatrics of my own general practice consists of trivia. I use the term humbly, well aware that, clinically, trivia must never be treated with triviality. The fact that these acorns may grow mighty oaks gives heart to those who accept general practice as it actually is, maintain a feeling of accomplishment, and see no humility in the fact that their training dealt with many things they no longer see or do. Many doctors, each with a mission in life, culled all those fascinating cases at the teaching center from a hoard of the clinically humdrum.

In the course of a busy practice it is somewhat difficult to classify each case and keep an accurate record. However, I utilized a modification of a code which appeared in *GP* in 1952[6] and obtained a more or less accurate profile of my practice during the year 1956. Services were coded as to whether they were house calls, office calls, etc. Each patient contact was coded under one of eleven categories as to specialty. I must admit that there were times when one's choice in this respect might have been a matter of controversy. However, I was easily able to separate the pediatric cases at any rate.

In this manner, in round numbers, there were some 9,100 patient contacts of one sort or another. Of these about 3,100 were contacts with patients of the pediatric age group and about 2,700 of these 3,100 were first visits for particular cases.

One of the most interesting facts was that visits for the nine most common causes constituted over 2,100 of the pediatric visits.

They were broken down as follows:

Routine well-child care and immunizations	1,002 calls
Common cold	270
Bronchitis	230
Tonsillitis	167
Otitis media	135
Simple nonspecific gastrointestinal upsets	113
Streptococcus sore throats	97
Acute nonspecific or viral sore throats	64
Simple diarrhea	51
Total	2,129

In other words, a large proportion of the pediatric patients was well children. Of those who were sick the vast majority had only some garden variety of simple illness.

What about the other 600 cases? Their variety was great but there were, for instance, no children with congenital gastrointestinal defects or congenital heart disease. There was not a single patient with meningitis and none with poliomyelitis, nor were there any diabetics. One child with leukemia was the only pediatric patient with malignancy (thank God) and his was the only death.

Where, then, lies the pleasure in providing the medical care for these children? Two thousand bellies palpated and not a Wilms' tumor or a neuroblastoma. Hundreds of urines checked, none with sugar. Four thousand testes were down or came down, not a hip was dislocated; there was no hydrocephalus, no blindness, and no mucoviscidosis. There may have been hundreds of "dull" cases but there were three thousand interesting patients.

General practice, pediatric or otherwise, is not for anyone whose enthusiasm must constantly be kept sharpened by the rare and unusual or difficult. On the other hand, your appetite for such work may be kept whetted by maintaining a constant alertness to the fact that one of your patients may, indeed, prove to fall into this class. In any event, a feeling of accomplishment will arise and peace of mind prevail when one comprehends that every "case" is a patient, a patient all your very own, for the moment at least.

KEITH HAMMOND, M.D.

Paoli, Ind.

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News and Notes

Dr. John Edwin Brown, Jr., Columbus, Ohio, died June 3, 1958, of a heart attack at the Columbus Children's Hospital, where he had gone for his morning ward rounds.

Dr. Brown had been an Associate Professor of Pediatrics at The Ohio State University since 1947. He was Chairman of the Board of Trustees of the Columbus Academy of Medicine. From 1941 to 1945, he served in the Army Medical Corps, reaching the rank of Major prior to discharge.

The following diplomates were certified by the **American Board of Pediatrics, Inc.**, at Cincinnati, Ohio, June 13, 14, 15, 1958.

Dr. Julius T. Adams, 130 Graystone Terrace, Apt. 3, San Francisco, Calif.

Dr. Philip Adler, 17193 Greenlawn Ave., Detroit 21, Mich.

Dr. Lewis Bruce Anderson, Jr., Billings Clinic, 2802 Ninth Avenue North, Billings, Mont.

Dr. Bailey C. Andrus, 315 Nichols Road, Kansas City, Mo.

Dr. Charles H. Bauer, 525 East 68th St., New York 21, N. Y.

Dr. James Harvey Belt, 6202 College, Indianapolis, Ind.

Dr. Robert Edward Bolinske, 4264 Beechlawn Road, Columbus 13, Ohio.

Dr. Edwin F. Buzan, 604 E. Broadway, Alton, Ill.

Dr. Harvey Lee Carter, U. S. Naval Hospital, San Diego 34, Calif.

Dr. Alfred Y. T. Ching, 1009 Granger St., Ann Arbor, Mich.

Dr. C. A. Cilella, 6334 N. Olcott Ave., Chicago 31, Ill.

Dr. Alan L. Cline, 516 Pontiac State Bank, Pontiac, Mich.

Dr. Bradford Philip Cohn, 500 Spruce St., San Francisco, Calif.

Dr. William R. Collins, Jr., 414 County St., New Bedford, Mass.

Dr. Maria Antoinette Crea, 3395 Scranton Road, Cleveland 9, Ohio.

Dr. Joseph Michael Daly, 234 East Southern Ave., Indianapolis, Ind.

Dr. Albert H. De Garmo, 6513 Cliffridge Lane, Cincinnati 13, Ohio.

Dr. Gerhard H. Dorgelo, 901 Helena St., Trail, British Columbia, Canada.

Dr. Nathan P. Eisenberg, Charminel Hotel, Columbus, Ohio.

Dr. James Joseph Englert, 6048 Montgomery Road, Cincinnati 13, Ohio.

Dr. Constantine John Falliers, 465 South Olive Way, Denver 22, Colo.

Dr. Mary Alice Vann Fox, 7400 Fairfax Road, Bethesda 14, Md.

Dr. Raymond S. Freeman, 5125 E. Yale Ave., Denver 22, Colo.

Dr. John Christian Gall, Jr., 902 South Lake, Miles City, Mont.

Dr. Robert David Gauchat, Department of Pediatrics, State University of Iowa Hospitals, Iowa City, Iowa.

Dr. Julius Andrew Gerlach, Jr., 14145 Pleasant Valley Road, Cleveland, Ohio.

Dr. James Vincent Glaser, 10703 White Oak Ave., Granada Hills, Calif.

Dr. Robert Francis Good, 348 Livingston Road, Dravosburg, Pa.

Dr. Robert Eric Greenberg, Department of Pediatrics, Syracuse Memorial Hospital, Syracuse 10, N. Y.

Dr. Herman Grossman, 1032 Woodland Ave., Oradell, N. J.

Dr. Alfred Hamady, 140 Capital Ave., N.E., Battle Creek, Mich.

Dr. Thomas A. Hanson, Madigan Army Hospital, Tacoma 99, Wash.

Dr. Birt Harvey, 3887 Corina Way, Palo Alto, Calif.

Dr. Ralph E. Haynes, 1400 Bland St., Bluefield, W. Va.

Dr. Clarence Ronald Higgins, Jr., Base Hospital, Castle AFB, Merced, Calif.

Dr. Cecil Byron Howard, Doctors Building, Tuckaleechee Pike, Maryville, Tenn.

Dr. Martin J. Kaplan, 730 Judson Ave., Highland Park, Ill.

Dr. John David Kaster, 955 Jackling Drive, Hillsborough, Calif.

Dr. Ingeburg G. A. Kultzen, 722 West Lodi Ave., Lodi, Calif.

Dr. Leslie W. Langley, Jr., Wahle Apts., Bourne Ave., Somerset, Ky.

Dr. Leslie Mackoff, 4115 University Way, Seattle 5, Wash.

Dr. Edward C. McKeon, Office for Medicare —Office of the Surgeon General (Army-9911) Washington 25, D. C.

Dr. Donald Norman Medearis, Jr., Harriet Lane Home, Johns Hopkins Hospital, Baltimore 5, Md.

Dr. Robert Bère Mellins, 102 S. Broadway, Tarrytown, N. Y.

Dr. Joseph Boxley Miller, Jr., 802 Grand Ave., Yazoo City, Miss.

Dr. Jeanne Elizabeth Nitchals, 2205 Beechmont Ave., Cincinnati 30, Ohio.

Dr. Clayton Norton, Rt. 1, Box 1, Arnold, Md.

Dr. Fred Pipkin, 4202 Poplar Level Road, Louisville 13, Ky.

Dr. Robert F. L. Polley, 840 Medical-Dental Building, 509 Olive Way, Seattle 1, Wash.

Dr. Franz Weston Rosa, U. S. Overseas Mission to Iran, APO 205, N. Y.

Dr. Joseph Hyman Rosenthal, 6 Tappan Lane, Orinda, Calif.

Dr. Agnes Jean Rovnanek, 45 Fort Douglas Blvd., Salt Lake City, Utah.

Dr. Louis Schwab, 6719 Hammerstone Way, Cincinnati 27, Ohio.

Dr. Jack G. Shiller, Bay Street, Westport, Conn.

Dr. David Leo Simon, 634 North Grand Blvd., St. Louis 3, Mo.

Dr. Arnold Miller Steinman, 5738 Wilkins Ave., Pittsburgh 17, Pa.

Dr. George Stephen Sturtz, 121 Mullin St., Watertown, N. Y.

Dr. Isabel Lai-Fong Szeto, 6681 Ridgeville, 2nd Floor, Pittsburgh, Pa.

Dr. Milton G. Tall, 198 Dumbarton Road, Baltimore 12, Md.

Dr. Allan Perry Thomas, 115 East South Temple, Salt Lake City, Utah.

Dr. Spencer Gwaine Thompson, Carle Clinic, Urbana, Ill.

Dr. James K. Turner, 101 S. Meramec, Clayton 5, Mo.

Dr. Richard Eugene Turner, 2110 Main St., Springfield, Ore.

Dr. James R. Upp, 148 St. Andrews Fairway, Biloxi, Miss.

Dr. Vlastimil Vrla, 311 Fir St., Park Forest, Ill.

Dr. S. Zoe Walsh, 47 West 75th St., New York 23, N. Y.

Dr. Raymond Arthur Weitemier, 2000 E. Main St., Richmond, Ind.

Dr. John H. Whitcomb, 21 East Wright St., Pensacola, Fla.

Dr. John Francis Wilson, Children's Hospital Research Foundation, Cincinnati 29, Ohio.

Dr. Lewis Grant Wilson, Department of Pediatrics, U.C.L.A. Medical Center, Los Angeles 24, Calif.

Dr. John Thomas Young, 4167th USAF Hospital, Travis AFB, Calif.

The following candidate passed the examination in Memphis, Tennessee, in March, 1958, but was not eligible to receive certificate until July 1, 1958.

Dr. Sheldon Kamin, c/o Mr. Sam Kamin, 5449 West Congress Parkway, Chicago 44, Ill.

SPECIAL FOREIGN CERTIFICATES:

Dr. Fe Canlas-Dizon, 2410 Jose Abad Santos Blvd., Manila, Philippines.

Dr. Rosario Carretero, 2157 O'Donnell St., Manila, Philippines.

Dr. Peter Wai Shuen Choy, 9 Stanley Beach Road, Hong Kong.

Dr. Liborio Garcia, 209 E. Fernandez, San Juan, Rizal, Philippines.

Dr. Heskel M. Haddad, 76 Katznelson St., Givataiim, Israel.

Dr. Bharat Bhushan Kumar, 42nd and Dewey Ave., Omaha 5, Neb.

Dr. Harish Mazumdar, 166 East 45th St., Brooklyn 3, N. Y.

Dr. Adoracion Concepcion Morales, 1241 Trabajo St., Sampaloc, Manila, Philippines.

Dr. Carlos Vallbona, 280 Aragon, Barcelona, Spain.

Dr. Pio G. Vera Cruz, Unisan, Quezon, Philippines.

Dr. Kishin Vishindas Wadhwani, Medfield State Hospital, Harding, Mass.

Dr. Kariagounder Manonmani, Kings County Hospital, Brooklyn 3, N. Y.

Dr. Priscila C. Reyes, 830 S. Wood St., Chicago 12, Ill.

Dr. Mahdy Makkia, 335 A/1 Rashid St., Bet-Lench, Baghdad, Iraq.

At the Annual Meeting of the **American Medical Association** in San Francisco in June, the following officers were elected by the Section of Pediatrics for the coming year:

Chairman: Wyman C. C. Cole.
Vice Chairman: Edwin Revere Cole.
Secretary: Arild E. Hansen.
Delegate: Walter B. Stewart.
Jacobi Fund Trustee: Hugh L. Dwyer.
Representation on Scientific Exhibits Committee: F. Tom Mitchell.

Dr. Milton J. E. Senn, Professor of Pediatrics at the Yale Medical School, was in Russia this past summer studying child care and rearing methods in the Soviet Republic. A Russian physician will be the guest of the Child Study Center at New Haven later in the year.

Dr. Robert H. Alway of San Francisco, Head of the Department of Pediatrics at Stanford University Medical School, has been appointed Dean of the Faculty. The Stanford Medical Center at Palo Alto, which will house the Medical School, is scheduled to be completed later this year.

Dr. Jerome Glaser of Rochester, New York, has been awarded the Albert D. Kaiser Medal for 1958 by the Rochester Academy of Medicine, for his "contributions to the science of medicine in the fields of allergy and pediatrics."

The **American Association for Cleft Palate Rehabilitation** will hold its Seventeenth Annual Convention at the Sheraton Hotel in Philadelphia on Thursday, Friday, and Saturday, April 30, May 1 and 2, 1959. This Association is composed of medical, dental and paramedical specialists who are interested in the rehabilitation of persons with cleft lips and palates.

The **University of Michigan School of Public Health** and the **University of Minnesota School of Public Health** will jointly hold an "*Institute on Perinatal Casualties*" for five days, Dec. 8-12, 1958, in Minneapolis, Minnesota. This Institute is jointly sponsored by the State MCH and CC Agencies of Michigan and Minnesota. It will be financed by a grant from the U.S. Children's Bureau. Each person selected by a State will have his travel expenses, tuition, lodging, and meals paid for as part of the Institute. Payment for expenses will be made by the University of Minnesota School of Public Health from funds provided by the Children's Bureau.

The Program will consist of a series of seminars and discussions. Faculty for the Program will be provided from the Schools of Public Health of the Universities of Michigan and Minnesota, and other resource people. The program will consist of such aspects of the problem of perinatal casualties as: Definition, Extent and Significance; Etiology; Prevention; Growth and Development; Coordination of Services including personnel involved, case finding, care, and follow-up; Perinatal Mortality Studies; Care of the Premature Infant; Specialized Programs (e.g., Mental Retardation, Cerebral Palsy, Congenital Heart Disease, etc.); Program Planning; Program Evaluation. The final program will be sent at a later date.

Each State in Regions V (Illinois, Indiana, Michigan, Ohio, Wisconsin) and VI (Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, South Dakota) will have the opportunity of selecting at least four staff members to send to the Institute (two staff members from MCH Program and two staff members from CC Program). Staff members selected should be those who are in a key position in program-planning and program-administration, consultation, and supervision within the State. Staff members should be selected on a *multi-disciplined basis* (e.g., physicians, nurses, social workers, etc.). States which would like to send a team of more than four people may possibly do so by special arrangement with Dr. Donald C. Smith, University of Michigan School of Public Health, or Dr. Helen M. Wallace, University of Minnesota School of Public Health. Personnel should be selected by the MCH and CC Directors of each state.

The American Psychosomatic Society will hold its Sixteenth Annual Meeting at Chalfonte-Haddon Hall in Atlantic City on Saturday and Sunday, May 2 and 3, 1959.

The Program Committee would like to receive titles and abstracts of papers for consideration for the program no later than December 1, 1958. The time allotted for presentation of each paper will be twenty minutes.

Abstracts, in octuplicate, should be submitted for the Program Committee's consideration, to the Chairman, Milton Rosenbaum, M.D., at 265 Nassau Road, Roosevelt, N. Y.

The *continuation medical education course for pediatricians* offered by the **University of Minnesota** on Sept. 23 to 25, 1958, will feature lectures, panels, and round-table discussions on "Advances in the Diagnosis and Management of Diseases in Infants and Children." The course will be presented by the full- and part-time faculty of the Department of Pediatrics of the University of Minnesota under the direction of Dr. John A. Anderson, Professor and Head. Guest participants will include Dr. Daniel C. Darrow, Kansas City, Dr. James N. Etteldorf, Memphis, and Dr. Waldo E. Nelson, Philadelphia.

The Northwest Pediatric Society's annual scientific meeting is being held on Friday, Sept. 26, 1958, at White Pine Inn, Bayport, Minnesota. All registrants for the Pediatric Continuation Course are welcome and are encouraged to arrange their schedule so that they might attend this meeting. Lodging and meal accommodations are available at the Center for Continuation Study.

Books

Directory for Exceptional Children, ed. 3. Porter Sargent Publisher, Boston, 1958, 320 pages. Price $6.00.

A most useful reference book for those seeking to learn about facilities for the care of exceptional children. It is divided into sections, listing by states facilities for children socially and emotionally maladjusted; orthopedically handicapped (cerebral palsy); mentally retarded; multiple handicaps; blind, deaf, psychiatric, and child guidance clinics; speech; and tutoring schools. Physicians are frequently asked for advice and information and an up-to-date reference directory such as this is a necessity in view of the rapid development in recent years of facilities for children with physical and emotional problems.

l'Hydrocephalie du nourrisson. Marc-Richard Klein, et al., Paris, 1958, Masson et Cie, 136 pages. Price 1,600 fr. (French).

A study based on 300 cases of hydrocephalus observed and operated upon by the author, neurosurgeon to the Hôpital des Enfants-Malades, and his associates. The necessity of operation before the brain structure has been damaged for too long a time is stressed. The various types of hydrocephalus are discussed. The author relies on coagulation of the choroid plexus as the operative procedure. Insistence is placed on a careful clinical study of the mental development before operative interference.

The Parents' Guide to Everyday Problems of Boys and Girls. Sidonie M. Gruenberg, New York, 1958, Random House, 363 pages. Price $4.50.

Mrs. Gruenberg, formerly Director of, and now Consultant to, the Child Association of America, is the author of some fifteen books for lay reading on children and family life. In a number, her husband, Benjamin C. Gruenberg, was co-author. She has the knack of writing in a style the public obviously finds satisfactory. Much of the new volume seems repetitious of earlier books and at times rather didactic.

Chirurgie préventive de la tuberculose ostéo-articulaire. R. Kaufmann, Paris, 1958, G. Doin et Cie, 174 pages. Price 2,000 fr. (French).

A monograph presenting the ideas of the author on the prevention of long immobilization for tuberculous osteoarthritis by early operative interference. The author's contentions are controversial and of little but academic interest in countries such as the United States, where tuberculosis of the joints has become almost a rarity following tuberculosis control.

Affections non congénitales de l'anus et du rectum chez l'enfant. Jean Duhamel, Paris, 1958, Masson et Cie, 264 pages. Price 3,600 fr. (French).

An excellent monograph on pediatric proctology that should be a valuable reference text. The author first describes techniques and then takes up in detail such conditions as ulcers, anal fissures, foreign bodies, prolapse, polyps, and malignant tumors. Each discussion includes details of treatment. The text has 110 illustrations.

Signs, Symptoms and Treatment of Certain Acute Intoxications, ed. 2. William B. Deichmann, Ph.D., and Horace W. Gerarde, M.D., Springfield, Ill., 1958, Charles C Thomas, Publisher, 154 pages. Price $3.75.

An enlarged, rewritten edition of this handy practical manual.

Editor's Column

PET PEEVES

UNDOUBTEDLY everyone is irritated by some pet dislikes in the use of the English language as he runs across them in a medical journal or text. It is nothing compared with those of an Editor who has to read the contributions in manuscript. These irritations seem to have a physiologic acceleration each year as the hot summer days come around. Regardless of the method employed, the accepted principle of all schools of psychiatry for getting rid of an emotional irritant is to "get it off one's chest." So here goes.

What irritates one may not irritate another. For example, our reaction was one of amusement at the choler and diatribes aroused in John Ruhräh by the word "pediatrician" rather than "pediatrist." "That bastard word" was his favorite expression of disgust. He was quite right etymologically. Nor could we be deeply stirred by John Howland's irritation over the use of the term "newborn" infant rather than the preferable "newly born." The frequent misuse of "ease" and "patient" in a manuscript no longer irritates us as it once did, and the reaction now is simply to use the blue pencil. We make no pretense of being a grammarian or a purist and frankly admit that our sins have been many. Fortunately, our two pediatric friends, Park White and Max Deutch, who have been contributing to the gaiety of life with their clever verses gently chiding the erudite *New England Journal of Medicine* for some editorial lapses, have been kind and generous enough to overlook the many for which we have been responsible. Perhaps less is expected of a midwestern Editor than of one from the "home of culture and beans." As an example of our illiteracy, we still have a confused hangover from our childhood days concerning the correct usage of "that" and "which." Although we have studied the correct usage many times, when it comes down to concrete choice we are still confused as to which the that usage applies—or is it to that the which?

We have had to give in and accept some of our peeves, although they still irritate. One is the use of the adjective "premature" as a noun—thus "prematures" when speaking of premature infants. As one of our academic friends warned us some twenty years ago, it was a losing fight for good English, although he agreed fully that "prematures" was bad English. Corruption breeds corruption. Not so long ago a manuscript was received in which the author used the term "premies" in the opening paragraph. It was returned with the suggestion that the author first learn to write English before attempting to write medical articles for publication. While we have had to resign ourselves to "prematures"—*premies!! d—— it, never!*

Another peeve is the increasingly incorrect use of the word "surgery," as, for example, "the child was sent to surgery." Perhaps "for surgery"

might be admissible, but the "to" calls for a place, such as a ward or service. Far better is the old-fashioned expression, "the child was transferred to the surgical service." We have yet to read "medicine was decided upon," although it is just as logical an expression.

One of our greatest peeves and irritants is not in the use of words, but the statement as a fact of a theoretical concept for which no scientific proof exists and which is probably incapable of proof. We have no objection to a discussion based on a theoretical concept. The objection lies in the statement of a concept as a fact. A glaring and frequent example is the "security of the womb" concept encountered in discussions by child psychiatrists. For example, a recent sentence was as follows: "When these are lacking he [the child] becomes fearful and in his anxiety seeks the shelter of the security he knew before birth." We ask how the writer—or anyone else—*knows* the unborn child *knew* security in the womb. The objection is not due to this concept by one school of psychiatrists—and Heaven only knows how many other schools disagree—being used as an explanation for certain forms of behavior in childhood, but to its being made as a statement of fact. What is worse is that it was not in a discussion for physicians, who probably would be aware that it reflected a theoretical concept, but in a discussion intended for popular reading. Incidentally, it might be pointed out that the basic fallacy in the concept lies in the fact that the intrauterine period of the life cycle is the most insecure point in the life of an individual. We have asked some of our psychiatric colleagues who hold to this concept to just what period of intrauterine life they refer, the embryo or fetus, and to just when in the womb the unborn child *knows* he is secure. When a statement is made as a fact, there must be supporting scientific data. We have never encountered any in this womb business.

Other peeves could be added, but as everyone undoubtedly has his own, and we already feel much better, it is a good time to quit.

BASIC RESEARCH PROGRAM

SOME three years ago the important report of the American Foundation on "Medical Research" stressed the necessity of basic fundamental research as contrasted with applied or "project" research. The bulk of the money available for medical research today is designated for project research. It is not an easy program to implement, as grants or gifts for medical research are likely to be designated for specific problems in which the donor has an interest.

A step forward has recently been made by the National Fund for Medical Education which has raised and awarded nearly 16 million dollars in the last ten years for the support of the medical schools. The fund is establishing a program through which funds from various sources, including Community Funds and the voluntary health agencies, can be channeled into basic research. It is hoped that it will not only advance basic research but help straighten out the present unbalanced situation between basic and project research.